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Review Article

Chiral Switch in Antidepressants: A New Frontier for Safer and More Effective Personalized Therapies: A Review

Nandula Lavanya, Rashmi Nelligare Gopalakrishna*

Department of Pharmaceutical Analysis and Chemistry, Sri Adichunchanagiri College of Pharmacy, Adichunchanagiri University, B.G. Nagara, Karnataka, INDIA.

ABSTRACT

Advancements in drug development emphasize enhancing efficacy, reducing side effects, and tailoring treatments to individual patient needs. Conventional antidepressant therapies often face limitations such as delayed onset of action, suboptimal efficacy, and undesirable side effects, leading to poor adherence and treatment resistance. These challenges underscore the need for more effective, safer, and patient-centered therapeutic approaches. Advancements in drug development now emphasize enhancing efficacy, minimizing side effects, and tailoring treatments to individual patient needs. This review explores the critical roles of chirality, single-enantiomer formulations, and personalized medicine in improving antidepressant therapy outcomes. A comprehensive literature analysis was conducted to assess how chirality affects drug-receptor interactions and pharmacokinetics. The review examined clinical data on single-enantiomer antidepressants, such as escitalopram, and evaluated personalized medicine strategies, including pharmacogenetic testing. Single-enantiomer formulations demonstrated superior efficacy and safety compared to their racemic counterparts. Isolating the active enantiomer improved receptor specificity, reduced off-target effects, and enhanced pharmacokinetic properties, including Absorption, Distribution, Metabolism, and Excretion (ADME). Personalized medicine approaches, particularly pharmacogenetic testing, enabled identification of genetic polymorphisms affecting drug metabolism and receptor sensitivity, thereby facilitating more precise and effective prescribing. Integrating chirality-based drug design with personalized medicine significantly advances antidepressant therapy. Single-enantiomer formulations and individualized treatment strategies offer improved therapeutic outcomes, reduced side effects, and greater predictability in clinical practice. Continued research and clinical adoption of these approaches hold promise for more effective and patient-centered management of depression.

Keywords: Chirality, Antidepressants, Single-Enantiomer, Therapeutic Effectiveness, Safety, Spectroscopic Drug Quality Control, Pharmacological Profiling, Personalized Medicine in Psychopharmacology.

Correspondence:
Dr. Rashmi Nelligare Gopalakrishna
Department of Pharmaceutical Analysis and Chemistry, Sri Adichunchanagiri College of Pharmacy, Adichunchanagiri University, B.G. Nagara-571448, Karnataka, INDIA.
Email: ng.rashmi85@gmail.com

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INTRODUCTION

Overview of Antidepressant Therapy

The mainstay of remedy for depressive disorders is antidepressant remedy, which no longer most effectively reduces signs however also enhances the overall functioning and good existence of individuals (Eap *et al*., 2021). Depression is a great intellectual health circumstance marked by means of disinterest in normal hobbies, exhaustion, and cognitive deficits that often seriously disrupt everyday functioning (Coelho *et al*., 2021). Antidepressant remedy focusses at the neurochemical imbalances connected to despair, particularly within the brain's serotonin, norepinephrine, and dopamine structures, even though the etiology of the disorder is complex and includes genetic, neurobiological, mental, and environmental elements (Hashim *et al*., 2010).

Beginning with the discovery of Monoamine Oxidase Inhibitors (MAOIs) and Tricyclic Antidepressants (TCAs) in the middle of the 20th century, the creation of antidepressant capsules represented a modern step forward in psychiatric therapy (Branch and Hutt, 2012). Despite their effectiveness, those first-generation tablets supplied extreme difficulties because of their dietary barriers and adverse effect profiles (Aturki *et al*., 2014) Newer medications like venlafaxine, sertraline, and fluoxetine are widely used today. They have expanded their role as antidepressants to treat various anxiety and depression disorders (Bhushan, 2024).

With traits in pharmacogenomics presenting a desire for more accuracy and successful treatment plans, new studies in antidepressant medicine keep broadening the scope of ability consequences (Hancu *et al*., 2021). Clinicians can create personalized treatment to maximize outcomes with the plan

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of coming across genetic markers connected to treatment metabolism, responsiveness, and reduce side effects (Hancu *et al*., 2024). For severe cases, like acute suicidality, new fast-acting medications, such as ketamine and esketamine, target glutamatergic pathways and provide quicker relief. Technology integration also improves adherence and makes it less complicated to identify troubles early in therapy (Hancu *et al*., 2024). For example, apps for medication reminders and mood tracking make it easier to stay on track. To ensure that the advantages of antidepressant treatment attain a variety of groups around the world, these developments must be combined with persevered projects to reduce stigma and access to mental health (Hashim *et al*., 2010).

Significance of Chirality in Drug Development

The life of non-superimposable reflect mirror images of a molecule, or chirality, (Figure 1) has a considerable effect on the pharmacodynamics and pharmacokinetics of medicinal drugs, making it an essential factor in drug improvement (Christodoulou, 2010). These mirror images, called enantiomers, can have different effects when they interact with chiral environments, such as proteins, enzymes, and receptors (Arenas *et al*., 2021). Most biological structures are chiral, so a molecule's interaction with its target is very specific. This means one enantiomer might produce the desired therapeutic effect, while the other could be inactive, less effective, or even harmful (Dash *et al*., 2017). To make medicines more effective and reduce side effects, it's important to understand and manage chirality during the drug discovery and development process. This stereospecificity is key to getting the best results (Kumari Rayala *et al*., 2022).

There are several well-known examples of how different enantiomers (mirror image forms of a molecule) can affect medicines differently. For example, thalidomide's one enantiomer worked well as a treatment for nausea and sleep issues, but the other caused serious birth defects (Coelho *et al*., 2021). This tragedy highlighted the importance of considering chirality when designing and testing drugs. Similarly, in the case of the popular anti-inflammatory drug ibuprofen, the S-enantiomer provides the anti-inflammatory benefits, while the R-enantiomer is less active but gets converted into the active form in the body (Liu *et al*., 2019).

Chirality also affects how drugs are Absorbed, Distributed, Metabolized, and Excreted (ADME) in the body. Enantiomers can interact with proteins in the gastrointestinal system differently, leading to varying absorption rates (Marques and Vale, 2022). For instance, propranolol, a beta-blocker, has two enantiomers that are absorbed and processed at different rates, which can lead to differences in plasma levels and how well it works (Nigam *et al*., 2020). Similarly, liver enzymes, such as cytochrome P450, tend to process one enantiomer more efficiently than the other, affecting how the drug is metabolized. This can impact drug dosing, half-life, bioavailability, and the creation of potentially harmful or active metabolites (Dash *et al*., 2017).

The capability to apply chirality for precision medicinal drugs will notably enhance the sector of pharmacotherapy through offering specialized treatments for lots of improvement as analytical and synthetic technologies (Sathpathy *et al*., 2024).

Rationale for Focusing on Single-Enantiomer Formulations

The capacity of single-enantiomer formulations to improve pharmacokinetic and pharmacodynamic characteristics, reduce side effects, and increase effectiveness is what motivates drug studies efforts (Sousa *et al*.,2021). Unlike racemic mixtures, which contain equal amounts of both enantiomers, single-enantiomer drugs include only the active enantiomer. Since drugs interact with their biological targets in stereospecific methods, growing formulations that completely consist of the therapeutically active enantiomer ensures safer and more predictable results for patients. This approach aligns with precision medicine to provide better outcomes (Hancu *et al*., 2024).

The main aim of improving healing efficacy, protection, and predictability at the same time as reducing side effects and maximising pharmacokinetics is the fundamental justification for targeting single-enantiomer formulation (Castrignano *et al*., 2018). Pharmaceutical developers are capable of generating their own drug treatments which might be steady with precision medicine concepts by making use of present day analytical and synthetic technology (Dash *et al*., 2018). As research uncovers more about the relationship between chirality and biological activity, the focus on single-enantiomer drugs is expected to grow. This will benefit patients and positively impact the healthcare system as a whole (Vashistha *et al*., 2022).

CHIRALITY IN ANTIDEPRESSANT DRUGS

Role of Chirality in Drug Mechanism of Action

The three-dimensional configuration of a molecule's atoms determines the way it interacts with organic objectives; chirality plays an essential role in determining how medicines work (Christodoulo,2010). Most biological systems, like enzymes, receptors, and transport proteins, are naturally chiral and can tell the difference between a drug's enantiomers (Arenas *et al*., 2021). Single enantiomer is frequently stronger or has an exclusive pharmacological profile than the other because of this stereospecificity. For example, the beta-blocker propranolol has R- and S-enantiomers, but only the S-enantiomer has strong beta-blocking properties (Nigam *et al*., 2020).

Chirality is important for drug-receptor interplay on account that a molecule's stereochemistry dictates how well it fits into a receptor correctly aligned. This specificity affects the drug's

potency, its ability to activate or block receptors, and the resulting biological and clinical effects (Kumari Rayala *et al*., 2022).

In comparison to racemic mixtures, single-enantiomer medications, like esomeprazole (the S-enantiomer of omeprazole), have improved healing overall performance and less interpatient variability (Eap *et al*., 2022). The growing recognition of chirality's pivotal role in pharmacological mechanism of action meditated on in this trend. Researchers can produce relatively selective medicines that better suit for the chiral man or woman of organic structures with the aid of concentrating on the stereochemistry of medicinal molecules in the nature of biological systems. Ultimately, this approach advances precision medicine and improves affected person outcomes (Hancu *et al*.,2021).

Impact of Chirality on Drug Metabolism and Pharmacokinetics

Chirality has a primary effect on pharmacokinetics and drug metabolism (ADME: absorption, distribution, metabolism, and excretion), which determines how medications behave in the body. Chiral drugs, that are regularly given in racemic mixtures (Figure 2). Containing equal amounts of enantiomers, may have exceptional pharmacokinetic and metabolic characteristics for each enantiomer (Coelho *et al*., 2021). Dosing schedules, protection, and therapeutic efficacy can substantially affect dosing schedules, safety, and therapeutic efficacy and its interaction (Sathpathy *et al*., 2024).

Due to stereoselective interactions with transport proteins and drug clearance enzymes, enantiomers often exhibit different rates of renal or biliary excretion. For instance, stereoselective glucuronidation in the liver causes the enantiomers of the nonsteroidal anti-inflammatory medication (NSAID) ketoprofen to be removed at varying rates. These differences in elimination kinetics can result in one enantiomer being retained for a longer period, which may have either beneficial or adverse effects (Castrignano *et al*., 2018). These stereoselective pharmacokinetic variations have significant clinical implications. Understanding and considering the impact of chirality on ADME (Absorption, Distribution, Metabolism, and Excretion) processes (Sousa *et al*., 2021) enable more accurate dosing and the development of safer and more effective medications (Liu *et al*., 2019).

CASE STUDIES OF CHIRAL ANTIDEPRESSANTS

Escitalopram: Citalopram's Active Enantiomer

The S-enantiomer of citalopram, a Selective Serotonin Reuptake Inhibitor (SSRI) commonly prescribed for anxiety and depression, is known as escitalopram. Research revealed that the S-enantiomer of racemic citalopram was primarily responsible for its therapeutic effects, while R-enantiomer contributed little and, in some studies, even interfered with the S-enantiomer's medication, brought about the development of escitalopram as a single-enantiomer medication (Bhushan, 2024). Clinical trials comparing escitalopram to racemic citalopram demonstrated showed advanced antidepressant efficacy at lower doses, resulting in a faster onset of action and fewer side effects. These advantages are attributed to the S-enantiomer's having higher binding affinity for the serotonin transporter, highlighting the importance of chirality in maximising antidepressant therapy (Eap *et al*., 2021).

Fluoxetine: Different Enantiomer Pharmacological Profiles

Fluoxetine, commonly marketed as Prozac, is another SSRI with enantiomers: R-fluoxetine and S-fluoxetine. Although the serotonin transporter is inhibited through both enantiomers, their pharmacological profiles and binding affinities differ. R-fluoxetine, for instance, demonstrates additional activity at sigma-1 receptors, which may contribute to its neuroprotective and anxiolytic effects (Vashistha *et al*., 2022). Although racemic fluoxetine is effective for treating anxiety and depression, research has shown the potential for using each enantiomer individually to enhance specific therapeutic outcomes or minimise adverse effects. For example, due to its sigma-1 receptor activity, R-fluoxetine has been studied for its potential to treat neuropathic pain and fibromyalgia. This example highlights how a deeper understanding of enantiomers' distinct characteristics can lead to broader medicinal applications (Christodoulou, 2010).

Venlafaxine: Stereoselective Metabolism in a Racemic Mixture

R- and S-enantiomers of the Serotonin-Norepinephrine Reuptake Inhibitor (SNRI) venlafaxine are given as a racemic combination. The pharmacokinetics and pharmacodynamics of these enantiomers vary. While the R-enantiomer additionally reduces norepinephrine reuptake, the S-enantiomer mainly inhibits serotonin reuptake. Notably, venlafaxine undergoes stereoselective metabolism to produce desvenlafaxine, its energetic metabolite, predominantly the S-enantiomer (Liu *et al*., 2019). Due to its more predictable effects and simplified pharmacokinetic profile, desvenlafaxine-marketed as a separate medicinal drug-is often preferred in clinical practice. This instance demonstrates how enantiomer-precise formulations and the pharmacological consequences of racemic antidepressants may be inspired the development of stereoselective metabolism (Nigam *et al*., 2020).

These case studies underscore the significant chirality impacts on the pharmacodynamics and pharmacokinetics of antidepressants, shaping their therapeutic profiles and guiding the development of more targeted and effective treatments (Dash *et al*., 2017).

Single-Enantiomer Formulations in Antidepressants

Therapeutic Efficacy of Single-Enantiomer Antidepressants

Single-enantiomer formulations maximise the pharmacological impact of the active form by concentrating only on it. For

example, escitalopram, the S-enantiomer of citalopram, has a higher affinity for the Serotonin Transporter (SERT), enabling it to inhibit serotonin reuptake more efficiently (Bhushan, 2024).

This targeted action reduces melancholy signs and stabilise mood, this specific concentration ensures greater serotonin availability in the synaptic cleft. Another important advantage of single-enantiomer antidepressants is their quicker onset of action (Kumari Rayala *et al*., 2022). According to research, escitalopram patients often see measurable enhancements of their melancholy symptoms after the first weeks of medicine, in preference to the lengthier durations wished for racemic citalopram. This rapid therapeutic effect is especially significant in an intense condition of severe depression, where prompt symptom relief is important to preventing major outcomes like suicidal thoughts. The active enantiomer's most appropriate binding effectiveness, which lets in a rapid serotonin, is frequently responsible for the quicker onset.

The therapeutic efficacy of single-enantiomer antidepressants is evident in their precise mechanism of action, faster onset, reduced side effects, and consistent treatment outcomes. These benefits, combined with their broad applicability, establish single-enantiomer drugs as a superior option for the treatment of depression and related disorders, advancing both patient care and the field of psychopharmacology.

Safety and Side Effect Profiles: A Comparative Analysis

Single-enantiomer formulations often outperform racemic mixtures in these areas due to their streamlined pharmacological characteristics (Sousa *et al*., 2021). By including new pharmacodynamic and pharmacokinetic interactions, the life of each active and inactive or antagonistic enantiomer in racemic drugs can make safety profiles more complicated. Single-enantiomer medications reduce those headaches by concentrating simply at the active enantiomer, providing a more secure and more consistent profile.

In racemic mixtures, the inactive or less active enantiomer contributes little to the intended therapeutic effect, often requiring higher doses to achieve efficacy (Nigam *et al*., 2020). Side effects are more likely to arise with better dosages, which may additionally have a negatively impact on patient compliance and treatment outcomes (Hancu *et al*., 2021). When compared to their racemic counterparts, such as citalopram, single-enantiomer medications, like escitalopram, achieve similar or superior efficacy at lower dosages, significantly lowering the burden of negative effects (Bhushan, 2024).

Single-enantiomer drugs provide significant safety and tolerability benefits over racemic mixtures. By eliminating the inactive or antagonistic enantiomer, these formulations reduce the risk of adverse effects, enantiomer-specific toxicity, and drug-drug interactions, while also enhancing patient adherence. These benefits make single-enantiomer drugs a safer and more effective choice in the management of depression and other chronic conditions.

Enhancing Therapeutic Effectiveness Through Chirality

Targeting Specific Receptors: How Chirality Improves Selectivity

Biological receptors are naturally chiral; chirality is essential for enhancing a drug's selectivity for specific receptors. Enzymes, ion channels, and neurotransmitter receptors possess asymmetric active sites that interact differently to each chiral drug's enantiomer (Arenas *et al*., 2021). This concept is illustrated by the "lock-and-key" analogy, which states that the simplest single enantiomer can perfectly suit the receptor's active site due to its spatial orientation. Reducing adverse effects and enhancing therapeutic precision depend on this selective binding, which ensures the pharmacological impact while minimising off-target interactions.

This is particularly important in cases where off-target receptor interactions can also result in undesirable side effects, that is particularly essential. For example, the S-enantiomer of the beta-blocker propranolol has greater selectivity for beta-adrenergic receptors, leading to the intended cardiovascular effects. On the other hand, the R-enantiomer has been associated with off-target actions that may produce adverse effects. The drug's safety and effectiveness are greatly expanded by setting apart the therapeutically active S-enantiomer, providing patients with a more tailored and effective treatment option.

Mechanisms Underlying Improved Patient Outcomes

Chirality enables these capsules to gain a specific fit with receptors, enzymes, or delivery proteins, minimizing off-target interactions. This specificity reduces the hazard of aspect outcomes and detrimental drug reactions, which are often linked to the non-active or counterproductive enantiomer in racemic combinations. By getting rid of these unwanted interactions, single-enantiomer formulations make certain that the therapeutic outcomes are maximized, leading to higher patient results.

The elimination of pharmacodynamic antagonism is any other critical thing. In some racemic drugs, single enantiomer may also counteract or lessen the healing results of the alternative. This antagonistic interaction now not only reduces drug efficacy but also introduces variability in patient responses. Single-enantiomer formulations, together with dexmethylphenidate for ADHD, put off this antagonism by means of isolating the energetic enantiomer. The result is a more regular healing impact, bearing in mind lower and more powerful doses, which improves symptom management and affected person compliance.

Extra receptor selectivity, optimised pharmacokinetics, elimination of pharmacodynamic antagonism, decreased detrimental consequences, and greater therapeutic accuracy are the mechanisms at the back of better affected person effects with single-enantiomer medications. Together, those elements assure that the medicine produces the favored effects with the fewest possible hazards, improving no longer simply scientific efficacy but also patient happiness and adherence. Single-enantiomer medicinal drugs are a vital step towards greater green and individualised healthcare remedies as our expertise of chiral pharmacology advances (Hancu *et al*., 2021; Bhushan, 2024).

Safety Considerations in Single-Enantiomer Antidepressants

Adverse Effects Linked to Chiral Differences

A medicinal drug's protection profile is greatly encouraged by using its chirality on account that extraordinary enantiomers of the equal molecule might also have interaction with organic structures in different methods (Vashistha *et al*., 2022). Variations in pharmacological and toxicological outcomes may also result from those factors. In racemic combinations, single enantiomer may additionally offer the healing advantage, even as the opposite may also nullify the acceptable effects of the energetic enantiomer or reason negative aspect consequences (Raikar *et al*., 2020). Improving medication protection and efficacy calls for an understanding of how chirality contributes to side results. In 1950's, the chemical thalidomide became utilised as a sedative and anti-nausea remedy. This is a brilliant instance of how chirality can influence terrible outcomes (Salido- Fortuna *et al*., 2024).

The intricacy of using racemic medications in medical practice is highlighted with the aid of facet consequences associated with chiral variations (Basso and Serban, 2019). The risks of the inactive or less desired enantiomer can jeopardise the safety and effectiveness of drugs, starting from teratogenicity and rancid-goal interactions to metabolism-related toxicities and DDIs (Caballo *et al*., 2015). By concentrating on the enantiomer with the first-class therapeutic and safety profile, single-enantiomer formulations offer an approach to lessen these hazards. This technique emphasises how critical chirality is to medication development and patient care (Castrignano *et al*., 2018).

Risk Profiles for Different Enantiomers

A chiral drug's enantiomers often have numerous pharmacological and toxicological profiles due to their differing interactions with biological targets, metabolic pathways, and transport systems. Because of these differences, where one enantiomer may contribute to therapeutic effects while the other may cause adverse effects or reduced efficacy. Understanding these risk profiles is essential for optimizing drug safety and effectiveness, particularly when developing single-enantiomer formulations (Wang *et al*., 2024).

The selectivity of enantiomers for biological receptors is one of the primary factors affecting risk profiles. Usually chiral, biological targets like enzymes and receptors might also bind single enantiomer more strongly than the other. For instance, the antidepressant effect of citalopram is produced by the S-enantiomer, escitalopram, which selectively inhibits the Serotonin Transporter (SERT) (Zhang *et al*., 2024). In contrast, the R-enantiomer contributes to side effects without enhancing therapeutic benefits and shows minimal activity at SERT. This discrepancy highlights the importance of selecting the enantiomer with the optimal receptor selectivity for minimize off-target effects and enhance the therapeutic index.

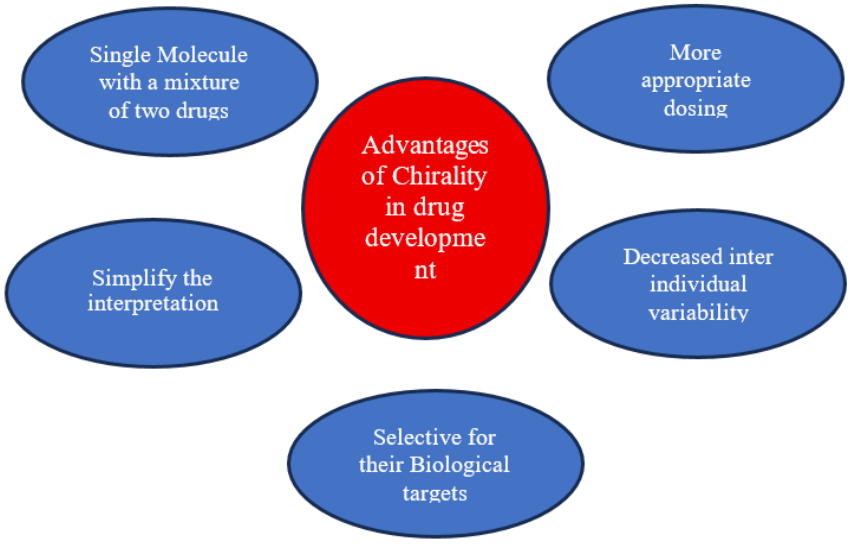

Figure 1: Advantage of Chirality in Drug Development.

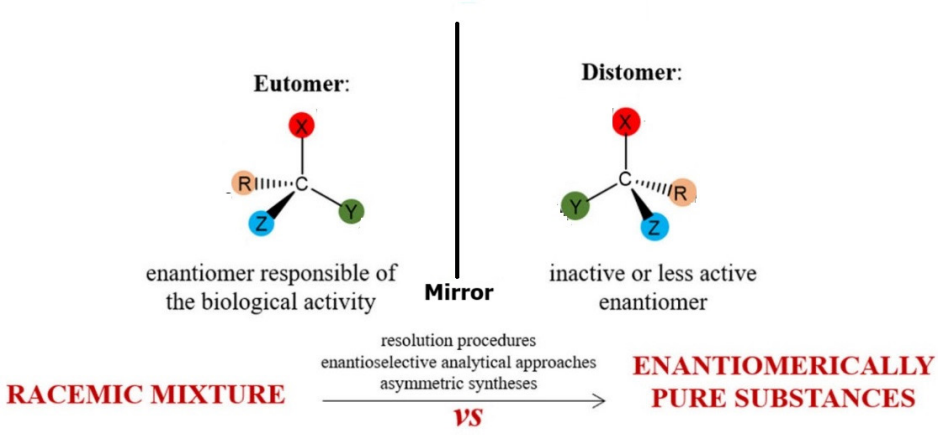

Figure 2: Importance of Chirality in Drug Activity.

The risk profiles of distinct enantiomers are shaped by receptor selectivity, metabolic pathways, antagonism potential, off-target interactions, and pharmacokinetic characteristics (Gumus *et al*., 2022). In order to design safer and more effective treatments, it's imperative that drug developers take these distinctions into account. By strategically lowering the risk associated with inactive or risky enantiomers, single-enantiomer formulations improve affected person safety and therapeutic effects. As research in stereochemistry advances, a deeper understanding of enantiomer-specific risks will further refine clinical practice and therapeutic strategies (Jalakam *et al*., 2020).

Regulatory Standards and Safety Protocols

Pharmaceutical tracking is based on safety approaches and regulatory standards, which ensure that medicines remain high-quality, secure, and effective over the course of their lives. National and international regulatory bodies establish these frameworks to direct the creation, authorisation, and publish-market surveillance of pharmaceuticals (Vashistha et al., 2024). These companies aim to protect the public health and promoting innovation in the pharmaceutical sector by establishing strict guidelines and standardized procedures. One of the key regulatory requirements is the need for preclinical and clinical testing before a drug is approved for market use (Jalakam *et al*., 2020).

A tiered method to drug development is required by organizations like the European Medicines Agency (EMA), the U.S. Food and Drug Administration (FDA), and others. This includes preclinical studies in labs and on animals, followed by using clinical trials on human participants (Wang *et al*., 2024). These assays are meant to evaluate pharmacokinetics, safety, and efficacy. For instance, Good Clinical Practice (GCP) guidelines, which assure data integrity as well as protect participants' rights, and well-being, have to be observed all through scientific studies. Getting regulatory approval depends on adhering to these procedures (Gumus *et al*., 2022).

For example, the E6 guiding principle on GCP from ICH has emerged a widely recognized standard for clinical studies. Additionally, safety approaches address emergency utilization instances and specific populations, requiring specialised regulatory approaches. For instance, physiological variances may additionally cause variable drug responses in pediatric and geriatric populations. Certain studies are required through regulatory bodies to evaluate safety and dosage in these groups. Similarly, to facilitate access to vaccines and treatments during crises like the COVID-19 pandemic, regulators established expedited pathways, such as Emergency Use Authorizations (EUAs) (Salido-Fortuna *et al*., 2024).

Improved post-market monitoring was introduced to these pathways which will swiftly address any emerging safety issues. For medicines to be safe, effective, and of high quality, safety protocols and regulatory standards are essential (Caballo *et al*., 2015). They encompass worldwide harmonisation, post-market surveillance, manufacturing quality, and preclinical and clinical evaluation. Regulatory bodies protect public health and promote innovation in drug studies by implementing these requirements.

Pharmacological Profiling of Single-Enantiomer Antidepressants

Enantiomer-Specific Efficacy and Toxicity Profiles

The specific methods that enantiomers interact with chiral biological structures; their efficacy and toxicity profiles can vary significantly. The differences that enantiomers interact with target receptors, enzymes, and metabolic pathways might vary because they may reflect distinct structural orientations (Basso and Serban, 2019). Understanding these differences is crucial for drug development to optimize therapeutic outcomes and reduce side effects. Enantiomers differ in their affinity for target receptors, leading in variations in efficacy. When it involves citalopram, as an example, the S-enantiomer (escitalopram) has a higher affinity for the Serotonin Transporter (SERT) than the R-enantiomer, which indicates lower activity. Escitalopram's therapeutic efficacy is accelerated by means of this selective binding, which

additionally makes it an extra effective antidepressant with fewer side effects. By identifying and isolating the active enantiomer, drug developers can improve clinical outcomes and reduce the dosage required to achieve the desired effects (Zhang *et al*., 2024).

The non-active enantiomer in a racemic mixture, however, can have little or no therapeutic efficacy in some cases, may even counteract the effects of the active enantiomer. For instance, both R- and S-enantiomers are found in racemic albuterol, commonly used to treat allergies. The S-enantiomer has been connected to pro-inflammatory and broncho-constrictive reactions, whereas the R-enantiomer acts on beta-2 adrenergic receptors to induce bronchodilation. These challenges have been resolved by the development of single-enantiomer formulations, including levalbuterol (R-albuterol), which offer better protection and efficacy profiles.

The complexity of chiral drug action and metabolism is highlighted by the specific efficacy and toxicity of the enantiomers. Although single enantiomer may have good therapeutic effects, the other may have negative side effects or be less effective. A key step in overcoming these challenges is the development of single enantiomer formulations, leads to safer and more accurate drug therapy. The ability to create and optimize enantiomer-specific drugs will improve patient care as our knowledge of chirality and pharmacogenomics continues to advance.

Translational Research and Preclinical Models

From 2010 to the present, translational research and preclinical models have advanced significantly due to advances in technology and a deeper understanding of human biology. Through their ability to bridge the gap between laboratory research and clinical application, these innovations have revolutionized drug discovery, disease modelling, and therapeutic interventions. The application of innovative technologies like CRISPR gene editing, artificial intelligence, and microfluidic systems, the development of preclinical models like patient-derived xenografts, organoids, and artificial organs, the integration of personalised medicine are important areas of advancement. These developments (Table 1) have enhanced the precision and efficiency of preclinical research but have also paved the way for more tailored and effective therapies in clinical settings.

Future Perspectives

Preclinical models and translational research have a promising future, with persevered developments to further revolutionize personalised medicine and drug development. As technologies like artificial organ structures, CRISPR gene editing, and artificial intelligence strengthen and provide increasingly individualised and precise insights into toxicity, therapeutic efficacy, and disease mechanisms. By considering quite a few affected person demographics and environmental variables, the integration of Real-World Evidence (RWE) and Real-World Data (RWD) will enhance the precision of preclinical models and make drug testing more scalable and predictive. Furthermore, the developing use of humanised models inclusive of advanced genetically modified animals and patient-derived organoids will improve the translation of findings to human clinical trials by bridging the gap between *in vitro* and *in vivo* testing. The convergence of these technologies will accelerate the invention of revolutionary treatments, reduce the drug development timeline, and optimize the safety and efficacy of therapies, ultimately providing patients with more effective and tailored treatment options.

Table 1: Year-wise transistional research with advanced preclinical models.

Year	Development in Translational Research	Key Advances in Preclinical Models
2018	Increasing emphasis on microbiome research and its influence on drug metabolism and disease.	Introduction of microbiome-based preclinical models to study the effects of the gut microbiome on disease processes and drug response.
2020	Focus on COVID-19 therapeutic research, including vaccine and antiviral drug development.	Development of humanized mouse models specifically for COVID-19 to test potential vaccines and treatments.
2021	Major strides in gene therapies and RNA-based drugs, such as mRNA vaccines and gene editing technologies for genetic diseases.	Emergence of humanized animal models for testing mRNA vaccines and evaluating immune responses.
2022	Continued expansion of AI/ML applications in drug discovery, with a focus on drug repurposing and optimizing clinical trial designs.	Increased use of AI-generated predictive models to simulate drug interactions and efficacy, reducing reliance on traditional animal testing.
2023	Growth of Real-World Evidence (RWE) and Real-World Data (RWD) in clinical research, impacting regulatory decision-making.	Focus on organs-on-chips and microfluidic devices as preclinical models for high-fidelity disease modeling and drug testing.
2024	Integration of regenerative and gene editing technologies in clinical trials, especially in oncology and genetic disorders.	Development of personalized preclinical models using patient-derived cells and tissues to simulate specific genetic mutations in disease models.

CONCLUSION

In conclusion, our understanding of disease biology and drug development has significantly improved over the last ten years due to the ongoing development of translational research and preclinical models. Innovations in technologies such as gene editing, artificial intelligence, and humanized models have made the drug discovery process more precise, efficient, and personalized. In addition to increasing the predictive capability of preclinical studies, these advancements are facilitating the faster conversion of findings into medical programs, raising the chance of greater individualised and efficient treatments. These technologies enduring the improvement of an extra patient-centered medical future, promising breakthroughs in the management of a wide range of complex diseases.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICAL APPROVAL

animals are not involved in the review.

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