ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/IJISRT24MAY1325

Therapeutical Potential of 5-HT6 of Receptor Modulation in Neurological and Psychiatric Conditions

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Abstract:- This review examines the pharmacological effects of targeting 5-HT6 receptors, a subtype of serotonin receptors found primarily in the hippocampus. These receptors are essential for synaptic function, functional plasticity and various cognitive functions such as learning and memory. The review synthesizes the existing literature to investigate the potential therapeutic use of drugs targeting 5-HT6 receptors in neurological and psychiatric conditions, including Alzheimer's disease, schizophrenia, depression, anxiety, neurodegenerative diseases and pregnancy mood disorders. Although some preclinical studies suggest positive precognitive effects, these results have often conflicted with clinical research; therefore more work needs to be done on drug classification and therapeutic effect as well as dosage considerations.

Keywords:- *5-HT6 Receptors, Serotonin, Pharmacology, Cognitive Function, Neurological Statics. , Psychiatric Disorders.*

I. INTRODUCTION

5-HT6 receptors, predominantly located in the hippocampus, represent a subclass of serotonin receptors. They participate in synaptic activity and functional plasticity in CA3/CA1 hippocampal connections and are involved in learning, memory, mood and behaviour. 5-HT6 receptor blockade results in precognitive effects in rodents with neurodegenerative psychiatric disorders and neurodegenerative diseases, as demonstrated in studies [1] and [2]. Clinical trials evaluating 5-HT6 receptor antagonists for treating cognitive impairment in Alzheimer's disease and other neurological disorders have produced disappointing results [3]. 5-HT6 receptors in the spine have been linked to diabetic neuropathic pain and related cognitive impairment, and hindering their constitutive activity with inverse agonists or interrupting the 5-HT6 receptor-mTOR interaction might offer a potential treatment approach. This compound holds promise as a therapeutic target for various neurological and psychiatric conditions based on pharmacological research. The inconsistent clinical effectiveness necessitates additional research on drug categorization and its impacts [5-7]. The 5-HT6 receptor, predominantly present in the brain, is primarily linked to learning, memory, therapeutic effects and mood regulation functions. 5-HT, often referred to as serotonin, significantly contributes to psychological processes. Ramos et al.'s research examines the impact on mood regulation, appetite, sleep, and cognition. The 5-HT6 receptor plays a role in mood regulation and emotional processing as shown in Figure No. 01.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/IJISRT24MAY1325

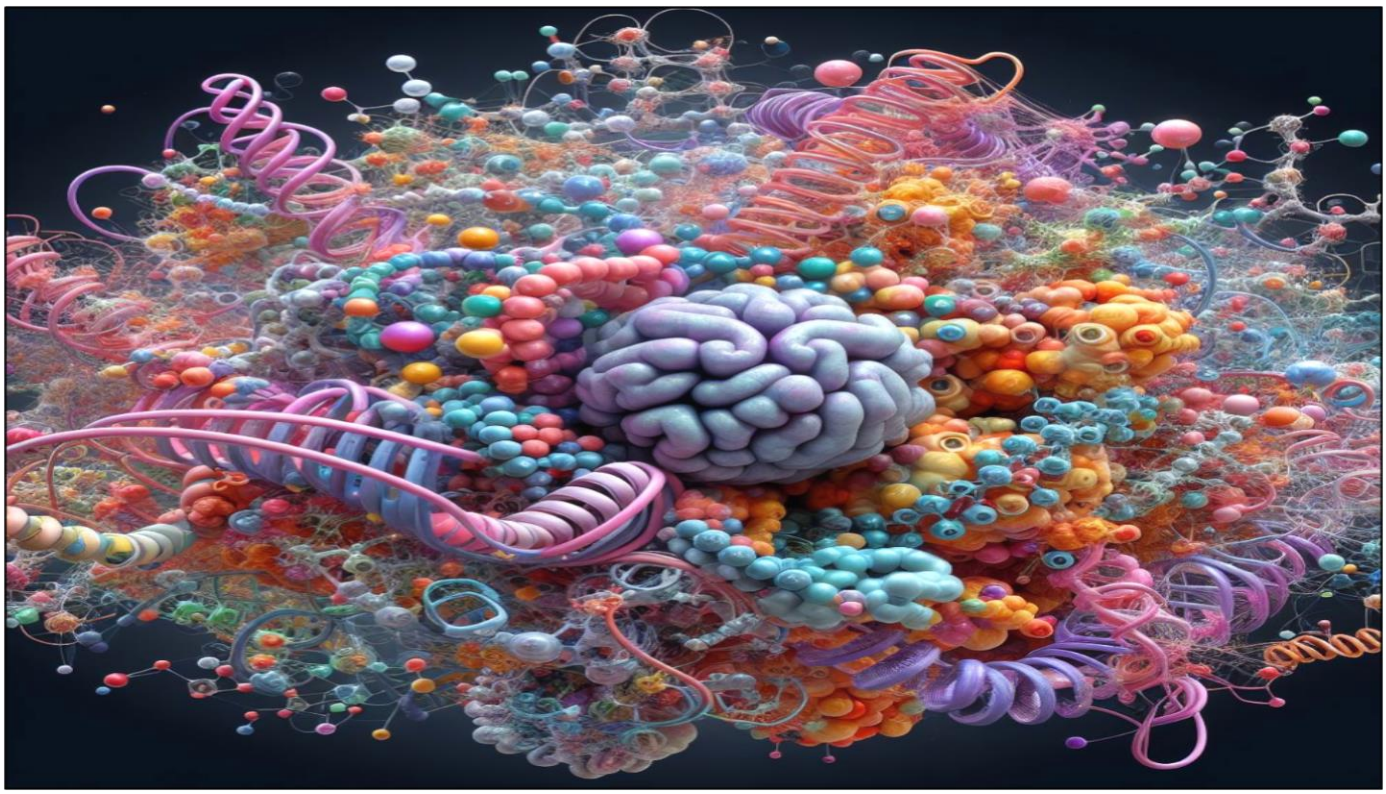

Fig 1:The 5-HT6 Receptor Involves Various Receptors found in the Brain and Binding around the Brain Receptors, Particularly in Regions Involved in Learning, Memory, and Mood Regulation Created with Copilot.design.com

In mood disorders like depression and anxiety, a change in this receptor's expression or function has been noted (Ana B. Ramos, 2019). The potential applications of 5-HT6 receptor-targeting drugs in neurological and psychiatric diseases are worth examining in depth [8]. The distributions of histamine and serotonin in the brain differ, as indicated in Figure No. 2.

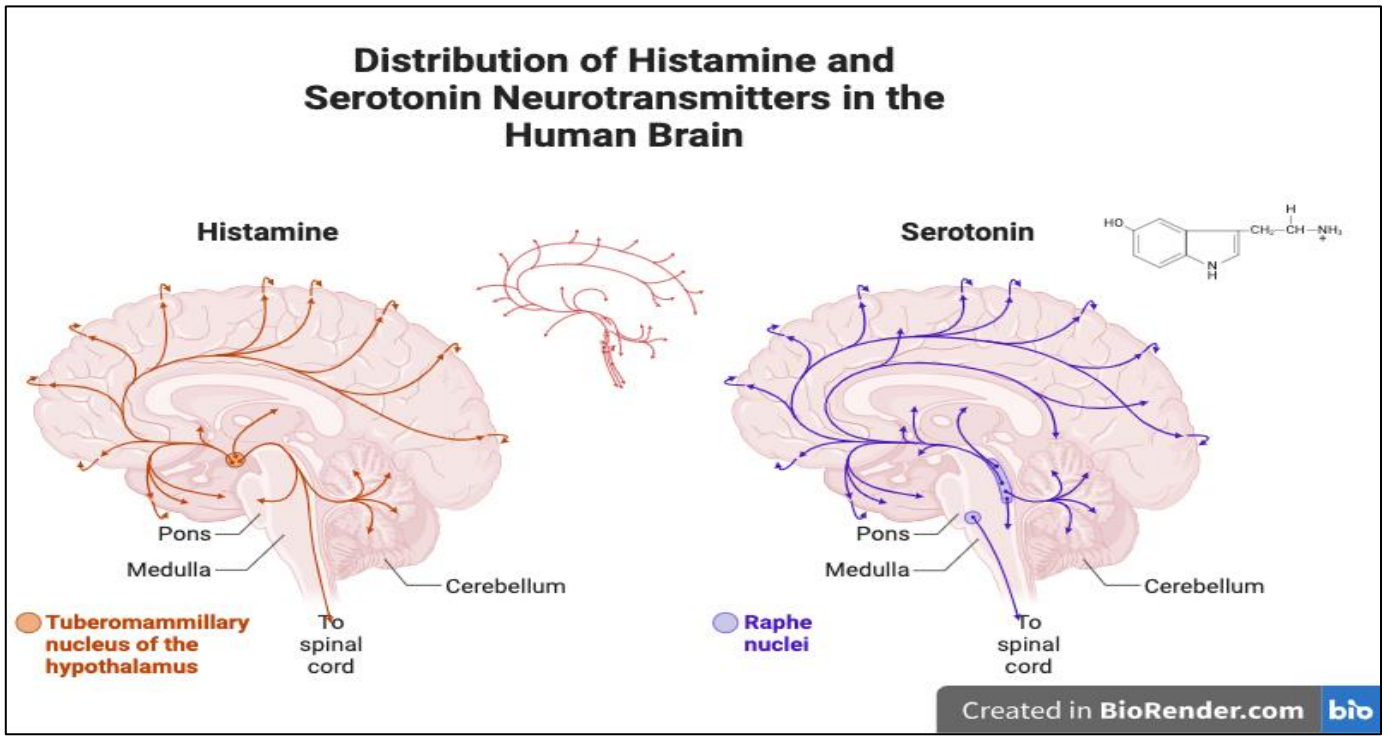

Fig 2: Distribution of Histamine and Serotonin Neurotransmitters in the Human Brain

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The main location of histamine-immunoreactive cells is in the ventral part of the posterior hypothalamus and the mammary core region [9]. Histamine fibres extend to the median eminence, diagonal area of Broca's nucleus, caudate-putamen complex, and cortical structures in the di- and telencephalon [10]. Unlike noradrenergic fibres, serotonergic fibres are abundant throughout the brain and possess unique distribution patterns. The thalamic nuclei, hypothalamic nuclei (most parts), amygdaloid basal complexes, lateral septal nuclei, hippocampus, nucleus accumbens, olfactory bulb, and cortex all contain these structures. In the cerebral cortex, the density of serotonergic fibres decreases rostrally to caudally [11]. The distribution of histamine and serotonin in the brain is detailed through these findings.5-HT6 receptor-targeting drugs were investigated for their ability to enhance cognitive decline in ageing, Alzheimer's disease, mild cognitive impairment, and other neurodegenerative disorders [12](Ramírez, 2013). Alzheimer's disease: The 5-HT6 receptor is thought to modulate the release of neurotransmitters and synaptic transmission in brain regions affected by Alzheimer's disease [13]. In the central nervous system, the 5-HT6 receptor plays a pivotal role in neurodevelopmental processes such as neuronal migration and brain circuit refinement.5-HT-6 receptors can be searched for in Medline 5-HT6 receptors gained widespread interest following initial studies on their cloning from 1993 to 2012. 540 studies over the last 20 years have examined receptors from various perspectives, including pharmacological, physiological, behavioural, and biochemical ones Figure no 03 shows that (Ramírez, M.J., 2013).

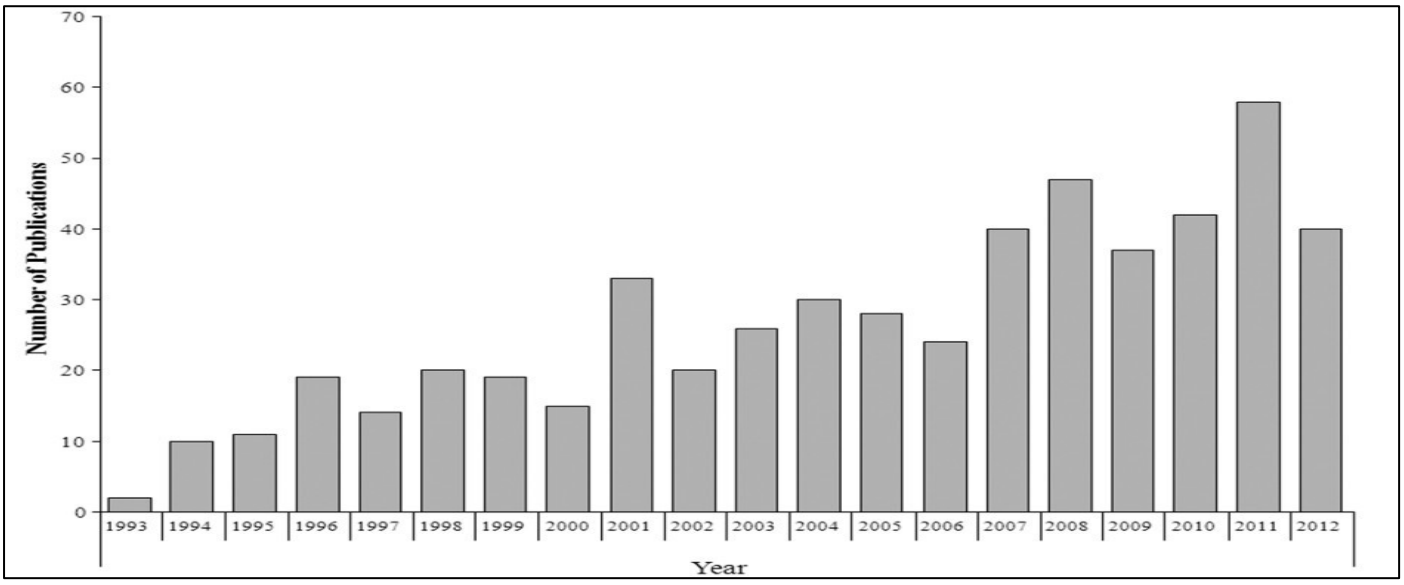

Fig 3: No of Publication vs Year

The second most frequent group of docking point values falls between -6 and -4, with values ranging from -6 to -4. The activity of CDK5, MARK4, ROCK I, and ROCK compound bound to 5-HT6R are compared. The above graph shows that the II targets have a slightly larger number of compounds with docking points between -10 and -8, while also having a higher proportion of compounds with docking points between -4 and -2 shown in Figure No 04 (2022).

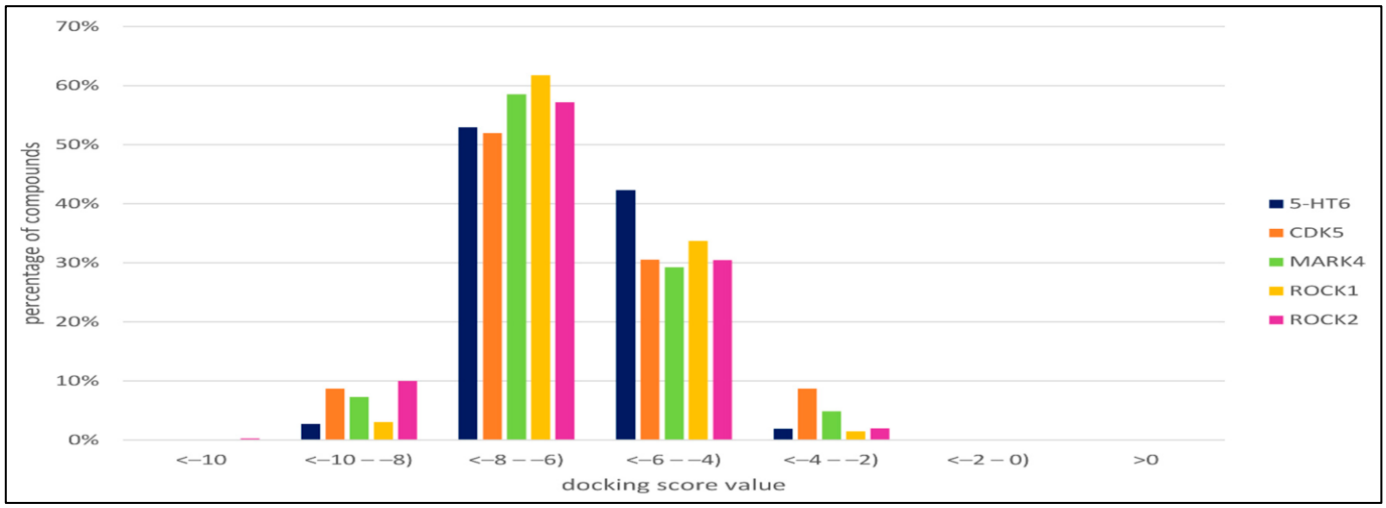

Fig 4: Percentage of Compounds vs Docking Score Value

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/IJISRT24MAY1325

Positioned as a potential tool to enhance cognitive function in AD patients, the receptor's role is in modulating neurotransmitter release. Alzheimer's disease is marked by progressive cognitive deterioration, neurodegeneration, and deficits in cholinergic and glutamatergic signalling [14]. In Alzheimer's disease, the 5-HT6 receptor is suspected to regulate neurotransmitter release and synaptic transmission in the brain. The effects of 5-HT6 receptor-targeting drugs on cognitive improvement and dementia symptom relief in Alzheimer's patients have been examined both as sole treatments and in conjunction with other pharmaceutical agents. 5-HT6 receptor modulation may benefit Alzheimer's patients by improving cognitive function and slowing disease progression. 5-HT6 antagonists like idalopirdine have been prescribed in doses ranging from 10 mg to 90 mg daily. Schizophrenia: Disturbances in serotonin neurotransmission, including changes in 5-HT6 receptor function, may be involved in the pathophysiology of schizophrenia, offering an opportunity for symptom control [15].

Schizophrenia, marked by perceptual, cognitive and behavioural aberrations, is a multifaceted mental illness. 5-HT6 receptor dysfunction in serotonin neurotransmission plays a role in the development of schizophrenia [16]. 5-HT6 receptor antagonists are under investigation for their potential antipsychotic effects that enhance cognitive functions in schizophrenia, including improvements in working memory and executive functions. 5-HT6 receptor targeting may alleviate cognitive decline and negative symptoms in schizophrenia, according to some research. 5-HT6 receptor modulators' impact on cognitive function in schizophrenia exhibited diversity.5-HT6 receptor antagonists are typically administered in doses ranging from 5 to 60 mg daily. Some researchers suggest the potential of HEC30654 to treat mood disorders, like depression and anxiety, due to its impact on mood regulation and emotional modulation at the receptor level. It modulates stress responses and emotions [17]. 5-HT6 receptor-targeting drugs may aid in treating depression and anxiety disorders by enhancing cognitive abilities and regulating emotions. 5-HT6 receptor antagonists have shown effectiveness in combating cognitive decline in Alzheimer's disease based on clinical study findings [18]. 5-HT6 receptor agonists and antagonists exhibit pro-cognitive, anxiolytic, and antidepressant effects in animal studies[19]. New derivatives of MST4 have been developed as potent 5-HT6 receptor antagonists with promising in vitro and in vivo properties [20]. 5-HT6 receptor-targeted drugs have shown potential as adjunctive treatment for depression and anxiety disorders, possibly due to effects on cognitive function. and emotional regulation. 5-HT6 receptor activation exhibits neuroprotective benefits against oxidative stress and excitotoxicity, potentially treating neurodegenerative disorders (Figure 5). 5-HT6 receptor activation offers neuroprotection against oxidative stress and excitotoxicity. 5-HT6 receptor agonist EMD-386088 and antagonist SB-399885 shielded against Aβ neurotoxicity via decreasing ROS and averting neurite outgrowth impairment shown in figure No 05[21].

Fig 5: 5-HT6 Receptor Agonist EMD-386088 and Antagonist SB-399885 Shielded Against Aβ

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5-HT7 receptor activation with small molecule ligands elevated PDGFRβ expression, shielding neurons from NMDA-triggered neurotoxicity [22]. Additionally, 5-HT6 receptor-targeted treatments were examined for their potential to mitigate the advancement and damage associated with neurodegenerative diseases like Alzheimer's and Parkinson's. 5-HT6 receptor targeting drugs' safety during pregnancy and lactation remains uncertain. Before getting any medication, pregnant or breastfeeding women must consult their healthcare provider. Several studies have examined the function of the 5-HT6 receptor during pregnancy and lactation. Malnourished animals were found to have greater neuronal activation in regions of the food reward system in response to a 5-HT6 receptor agonist [23]. Feeding serotonin (5-HT) precursors during pregnancy and lactation increases 5-HT production and affects maternal energy metabolism in the liver and mammary gland [24]. 5-HT precursor intake during pregnancy in sheep results in heightened 5-HT production and influences calcium transporter gene expression in the mammary gland and bone resorption markers in the femur [25]. 5-HT system alterations in lactating mice include a decrease in dorsal raphe nucleus immunoreactivity and an increase in serum 5-HT levels. 5-HT-involving selective serotonin reuptake inhibitors (SSRIs) have therapeutic roles in pregnancy and postpartum depression-related lactation mood regulation [26]. 5-HT6 drugs can be classified based on their binding affinities Full agonists elicit a response identical to the natural ligand when bound to the receptor. These receivers are fully activated and operate with high efficiency. Full agonist WAY-181,187 exhibits maximum receptor response.WAY-181187. • E-6837. • 2-ethyl-5-methoxy-N,N-dimethyltryptamine. 466, WAY number – 208. Here 5-sulfonamide derivative of Partial agonists binds to receptors and elicits less than the maximum response, even upon full receptor occupancy. Partial agonists exhibit agonistic and antagonistic effects depending on the context, with lower efficacy than full agonists. Submaximal responders and partial agonists like E-6837 tone down responses.

- E-68801.
- E-6837.

386.088 EMD
Idalopirdine, an antagonist or inverse agonist, potentially provides symptom relief by blocking or reversing receptor activation.
• ALX-1161
• AVN-211
• BVT-5182
• BVT-74316
• Cerlapirdine-Select
Idalopirdine specifically targets certain receptors.
Intepirdine acts as a selective antagonist.
5-HT6 and EGIS-12233 mixed with 5-HT7
Intepirdine is a drug that blocks specific receptors.
• Landipirdine
• Sertindole, olanzapine, asenapine, and cloz
• WAY-255315, Rosa Ruggosa.

- Latrepirdine (non-selective) and analogues.
- MS -245
- PRX-07034
- SB-258 585
- SB-271 046
- SB-357 134
- SB-399 885
- SGS518
- Ro 04-6790
- Ro- 46

WAY-181187: Action: WAY-181187 is a potent and selective 5-HT6 receptor full agonist [27-28]. The rat frontal cortex, hippocampus, striatum, and amygdala experience noticeable upticks in extracellular GABA levels, while the nucleus accumbens and thalamus exhibit negligible changes. The influence on neurotransmitter levels in these areas is negligible [29]. Rodent studies indicate that WAY-181187 possesses therapeutic potential against depression, anxiety, and obsessive-compulsive disorder, but its cognition and memory-impairing properties should be noted. [30] The combination of WAY-181187 and haloperidol yielded the greatest improvements, marked by antidepressant effects and diminished anxiety. The co-administration of risperidone along with an agonist and antagonist yielded an anxiolytic response [31]. The 5-HT6 receptor is involved in cognition, memory, and mood regulation processes. WAY-181187, an inhibitor of this receptor, holds therapeutic potential for treating conditions linked to serotonin dysregulation, including Alzheimer's disease, schizophrenia, and mood disorders. 5-HT6 receptor antagonism is linked to enhanced cognitive abilities, specifically in learning and memory capacities [32].5-HT6 receptor blockade may provide neuroprotection in neurodegenerative diseases such as Alzheimer's [33]. 5-HT6 receptor antagonism has been linked to enhancements in learning and memory functions in cognitive disorders. WAY-181187 could be beneficial for cognitive disorders like Alzheimer's and mild cognitive impairment [34]. 5-HT6 receptor dysfunction linked to neuropsychiatric disorders, including schizophrenia and mood disorders, could be treated with WAY-181187. 5-HT6 receptor blocker WAY-181187 is a potential treatment for neurodegenerative disorders like Alzheimer's, Parkinson's, and Huntington's due to its neuroprotective effects. In vascular dementia and traumatic brain injury, the use of WAY-181187, which could modulate serotonin signalling pathways, could be considered for treating cognitive impairment. However, individuals with known hypersensitivity or allergic reactions to WAY-181187 or its components should not use it. Patients with significant liver or kidney dysfunction should be closely monitored when administered WAY-181187 due to its impact on serotonin signalling [35]. When administered with other serotonergic agents like SSRIs, SNRIs, or MAOIs, WAY-181187's

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potential to affect serotonin signalling increases the risk of serotonin syndrome. Patients with cardiovascular conditions like arrhythmias, coronary artery disease, or hypertension should exercise caution due to the potential impacts of serotonin on their heart functions. The safety of WAY-181187 during pregnancy and lactation remains unclear. Pregnant or nursing women should first consult a physician before using WAY-181187. WAY-181187's safety and efficacy in children have yet to be proven. Paediatricians should closely supervise the use of this substance in children and adolescents. 5-HT6 receptor antagonism enhances learning and memory functions. Alzheimer's disease, mild cognitive decline, and age-related cognitive decline could benefit from the use of WAY-181187 [36].]. 5-HT6 receptor abnormalities in neuropsychiatric disorders, including schizophrenia, depression, and anxiety disorders, are linked to serotonin signalling issues. We can test the effectiveness of WAY-181187 under these circumstances. 5-HT6 receptor blockade with WAY-181187 holds neuroprotective promise for Parkinson's disease, Huntington's disease, and neurotemporal dementia [37]. Other conditions associated with cognitive decline: WAY-181187 may also be considered for conditions characterized by cognitive decline such as vascular dementia and traumatic brain injury. E-6837: E-6837 is oral. drug 5-HT6 agonist designed for the treatment of obesity. At human 5-HT6 receptors, it functioned as a full agonist. E-6837, given orally, only temporarily suppressed appetite. 4-week E-6837 administration in rats led to a 15.7% weight loss, greater than the 11% loss observed with sibutramine. E-6837 maintained the weight loss after a 43-day hiatus, while sibutramine did not, resulting in a rebound effect due to a decrease in fat mass. . . . 50% reduction in plasma leptin led to a decrease in fat mass, and both plasma glucose and insulin levels dropped following a glucose tolerance test in E-6837-treated animals. E-6837-induced weight loss is linked to enhanced insulin sensitivity and superior glucose regulation [38-39]. Drug development compounds are specifically engineered to interface with biological targets like proteins, enzymes, DNA or RNA. Determining the intended function of a compound relies on identifying the target. E-6837, an agent that acts on the serotonin receptor and is used to treat mood disorders, was given orally at 30 mg/kg to obese rats and produced hypertrophy and sustained weight loss. At the rat 5-HT6 receptor, it acts as a partial agonist (Emax = 67%), while at the human receptor, it functions as a full agonist (pEC50 = 9.2, binding pKi = 9.1). In a rat-feeding model, the compound demonstrated greater prolonged weight loss than sibutramine [40]. A drug's indications describe the diseases it is used to treat, prevent, or diagnose. These indications for investigational compounds result from safety, efficacy, and mechanism evaluations during preclinical studies and clinical trials specific to particular disease states. (Fisas, Angels, August 2006) Databases like Clinical Trials Registries store information on clinical trials.

- **Clinical Use**: A compound's therapeutic use is determined by the ailments it addresses. The efficacy and safety of the investigated compounds are evaluated through preclinical studies and clinical trials for specific therapeutic indications. Until these studies are completed and regulatory approval is obtained, the clinical use of the compound is speculative.E-6801:Credit: E-6801 refers to the evaluation of the quality of fuzzy algorithms, especially the detection of overlapping clusters. In complex networks, [41] signifies a significant influence. The E function analyzes a cluster's internal connectivity in comparison to its connections with other clusters. Its effectiveness lies in its sensitivity to minor shifts in membership numbers, allowing for precise evaluation of clustering accuracy within known datasets. Experiments have shown that the modified E-function works well in evaluating overlapping clusters, and this function has the potential for further optimization of fuzzy clusters [42]. In specific applications, different devices and systems operate through distinct mechanisms. With the aid of recent technological advancements, radiofrequency ablation (RFA) successfully treats various diseases [43]. To enhance stability and eliminate knocking, target detection devices integrate electromagnetic mechanisms with permanent magnets [44]. The sensitive and fast-tripping mechanism of residual current switches is activated through the use of a coil and spring [45]. Similar to pianos, keyboards are intricately designed with hammer weights, jacks, and pads to facilitate unique playing styles and sensations. Effective resource management is ensured through the selection and combination of operational data by event management systems using processors [46]. Each mechanism fulfils a distinct role in enhancing player interactions and synchronizing resource usage. 5-HT6 receptor agonist E-6801 enhances recognition memory via modulation of cholinergic and glutamatergic neurotransmission [47]. In rodents, this compound demonstrated significant memory enhancement when given alone or in conjunction with acetylcholinesterase inhibitors or glutamate NMDA receptor antagonists [48]. E-6801's effectiveness in reversing object recognition impairments caused by scopolamine equals that of donepezil, suggesting its application in treating memory disorders [49]. Extensive studies on the effects of E-6801 on recognition memory indicate that it is effective in the treatment of cognitive and memory disorders, which requires further investigation in clinical settings [50]. The E-6801 indication covers innovative uses of devices and methods described in the research literature. The device includes an E1 protocol converter with pointer connections, a colour-coded pointer, an electronic indicator with laser and LED lamp, and a marker signal generator for controlling functions. It provides voltage protection and component identification using a condensed laser beam. All these inventions provide unique functions such as timely reflection of driving conditions [51]. This device offers energy conservation with distinct coloured lights [52], detection of light points [53], resistance to voltage fluctuation [54], and reliable detection without thermal damage [55]. The administration of E-6801 is contraindicated under various circumstances. The literature extensively documents contraindications for different medical procedures, including bariatric surgery, contraception, orthognathic surgery and MRI.

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- **Bariatric Surgery** is not recommended for individuals with psychiatric illnesses, addictions, or certain age groups [56]. For patients with diseases such as HIV, lactating women, smokers above 35, and those with certain health issues, combined oral contraceptives are not advised [57]. Despite idiopathic condylar resorption, orthognathic surgery is not always contraindicated but requires careful patient selection and monitoring [58]. Patients with implanted devices or clips are contraindicated for an MRI scan, while claustrophobia or obesity may pose relative contraindications that could affect the procedure's feasibility [59]. 5-HT6 receptor agonist E-6801 showed promising effects on rats' recognition memory. At doses of 1.25-10 mg/kg, intraperitoneally administered E-6801 enhances object exploration, reflecting memory improvement [60]. At doses of 2.5 and 5 mg/kg, E-6801 matched donepezil's effectiveness in reversing object recognition deficits induced by scopolamine, underlining its memory-enhancing capacity. [61]. E-6801 significantly enhances rodent recognition memory through cholinergic and glutamatergic neurotransmission modification [62]. 5-HT6 receptor agonist E-6801, shown to enhance recognition memory through cholinergic and glutamatergic neurotransmission modulation [63]. This compound enhances target recognition memory, particularly when co-administered with SB-271046, donepezil, or memantine [64]. E-6801 improved scopolamine-induced object recognition impairment as effectively as donepezil [65]. The study suggests E-6801's potential as a valuable tool for enhancing memory and treating cognitive impairments. This provides new opportunities for therapeutic interventions in memory disorders.EMD-386088 Function: EMD-386088, a 5-HT6 receptor agonist, exerts significant antidepressant and anxiolytic effects when administered intrahippocampally in rats [66]. This compound displays both antidepressant and anxiolytic properties based on its effects in the forced swim and anxiety-related tests. The selective 5-HT6 receptor antagonist SB-399885 inhibits the anxiolytic and antidepressant effects of EMD-386088, improving its mechanism of action [67]. EMD-386088 demonstrated to impact hippocampal 5-HT6 receptors in this study, may hold promise as a novel therapy for depression and anxiety disorders. Indications: According to research data, EMD-386088 holds great potential. Reducing caloric intake, regulating plasma glucose, and increasing plasma glycerol in obese rats have shown potential for reducing body weight and body fat [68]. EMD-386088 was found to have antidepressant and anxiolytic properties in rats, as indicated by reduced immobility, anxiolytic activity, punitive responses, and increased open-arm participation in behavioural tests [69]. The compound enhanced grain flow signal measurements by removing noise via empirical shape decomposition, reducing measurement errors to below 1.6% of the total grain weight [70]. EMD-386088's potential applications extend to obesity treatment, depression and anxiety relief, and precise signal processing.
- C**ontraindications**: Individuals allergic to EMD-386088 or its components should not use the drug. Requiring dose modifications or heightened surveillance, patients suffering from extensive hepatic or renal dysfunction should take drugs influencing the serotonin system with caution, such as EMD-386088[71]. 5-HT6 receptor targeting by serotonin receptors, including EMD, may influence cardiac function (-386088). Patients with arrhythmia, coronary artery disease, or hypertension should use the drug with caution due to their pre-existing cardiovascular conditions. Be cautious when combining EMD-386088 with serotonergic agents, as increased serotonin risk is a possible syndrome. Women who are pregnant or nursing should seek professional advice before counselling with EMD-386088 due to unknown safety implications [71-74]. Studies stress the significance of drug safety knowledge for pregnant and breastfeeding women. Consulting healthcare providers is crucial for personalized advice regarding aripiprazole usage and hereditary angioedema (HAE) during pregnancy and lactation, as insufficient data necessitates further studies to inform prescribers and patients on drug safety. Consulting healthcare providers is essential for the health and safety of both the mother and baby when using medications such as EMD-386088. The significance of specific contraindications for EMD-386088 relies on its pharmacological properties. There is no available safety and clinical trial data for it.
- **Dose:** 5-HT6 receptor agonist EMD-386088 exhibits potential for depression and anxiety treatment in preclinical research. Rats exhibited reduced immobility in the forced swim test after receiving intrahippocampal administration of EMD-386088, demonstrating its antidepressant-like effect [75]. In addition, it showed alarming activity in tests such as the Vogel conflict and elevated plus maze tests, which reduced punitive responses and increased the number of open trials [76]. 5-HT6 agonist did not affect motor coordination or distance travelled in other tests, suggesting a specific effect on mood-related behaviour [77]. The study implies EMD-386088 as a possible treatment option for depression and anxiety disorders.
- **Clinical Use:** EMD-386088, a 5-HT6 receptor partial agonist, has shown promising clinical potential in several studies Studies show that EMD-386088 has antidepressant properties through activation of the dopaminergic system, as evidenced by a reduction in immobility in the forced swim test [78-79]. 5-HT6 receptor stimulation by EMD-386088 might be responsible for its antidepressant effects after both acute and prolonged use [80]. EMD-386088 was effective in enhancing cognitive function in patients with schizophrenia [81]. EMD-386088's potential clinical uses in treating depression, anxiety, and cognitive dysfunction in schizophrenia-like conditions are increased due to its ability to influence the dopaminergic system, generate antidepressant effects, and enhance cognitive functioning.

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- **LSD:** 5-HT6 receptors are bound by LSD [82]. The high-affinity binding and activation of the 5-HT6 receptor by LSD is contingent on its binding to this receptor [83]. Replacing Asp106 in transmembrane domain III with asparagine decreases LSD's capacity to stimulate adenylyl cyclase [84]. A tryptophan mutation in transmembrane region III and the replacement of two residues in transmembrane region VI alter the 5-HT6 receptor's ligand binding site [85]. 5-HT6 receptor-ligand binding site improvements can be achieved by analyzing these interactions [86]. The 5-HT6 receptor is one of the serotonin receptors that interact with LSD. 5-HT6 receptor partially activates by LSD, leading to enhanced atrial contractions. 5-HT reuptake and neural changes induced by LSD may be mediated by negative feedback mechanisms via direct stimulation of central 5-HT receptors [87-88]. 5-HT6 receptor antagonists have shown potential for improving memory and reversing memory loss in Alzheimer's disease, making them promising candidates for treating cognitive impairment [89]. Exploring LSD's therapeutic potential in psychiatric patients and managing its cardiac effects in clinical settings depends on comprehending its interaction with the 5-HT6 receptor [90].
- **Contraindications:** The hallucinogenic drug LSD interacts with the 5-HT6 receptor, among other serotonin receptors. 5-HT6 receptor modulation in rats results in yawning, stretching and chewing [91]. 5-HT6 receptor antagonists' structural features crucial for antagonism have been elucidated through extensive study [92]. 5-HT6 receptor-targeting compounds have been suggested for treating schizophrenia-like symptoms found in select mental disorders [93]. 5-HT6 receptor antagonists' efficacy depends on the structure of the amine group next to the sulfonyl group [94]. because of the intricate influence of LSD on the 5-HT6 receptor and multiple physiological and pharmacological processes, it's crucial to be cautious about potential contraindications. 5-HT6 receptor agonists and antagonists' effects are the focus of the context. 5-HT6 receptor agonist WAY-181187 dose-dependently raised the firing rate of 5-HT neurons in the dorsal raphe nucleus of rats [100]. Nirogi et al. evaluated the safety and tolerability of SUVN-502, a 5-HT6 receptor antagonist, in healthy adults and elderly subjects using single doses ranging from 5-200 mg and repeated doses of 130 mg. 5-HT6 receptor effects by LSD need further investigation regarding the exact doses.
- **Clinical Uses:**5-HT2A interacts with LSD, a potent sensory-altering substance. . . receptor and not the 5-HT6 receptor [95]. 5-HT6 receptor holds the potential for treating dementia through the use of agonists or antagonists [96-97]. Clinical studies have proven LSD's therapeutic value in treating anxiety and mental health issues [98]. The perception-altering effect of LSD is primarily due to its agonistic action on the 5-HT2A receptors [99]. 5-HT6 ligand studies for dementia treatment show conflicting results and further research is needed to assess their impact on cognitive function and behaviour.

II. RESULTS

The review uncovered an extensive literature base exploring various treatment alternatives, including medications. 5-HT6 receptors are targeted for various neurological and psychiatric conditions. Based on pharmacological investigations, 5-HT6 receptors have been identified as crucial in cognitive enhancement, oxidative stress and excitotoxicity protection, neurotransmitter modulation, and emotion regulation. Preclinical results for Alzheimer's disease and schizophrenia treatments have shown promise but clinical effectiveness has been unpredictable. 5-HT6 receptor antagonists and agonists dosing and classification were explored in the literature.

III. CONCLUSION

5-HT6 receptor targeting holds therapeutic potential for addressing cognitive deficits and mood disorders linked to neurological and psychiatric conditions. Further research is required to clarify the mechanisms, improve drug classification and dosing, and overcome challenges discovered in clinical trials. 5-HT6 receptor targeting during pregnancy and lactation warrants further investigation for safety, efficacy, and synergistic possibilities with current therapies. 5-HT6 receptor targeting offers potential for neurological and psychiatric treatment developments.

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