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Preclinical Screening of Antidepressant Activity of Formulated Sertraline Hydrochloride-Loaded Solid Lipid Nanoparticles in Rats

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Objective: The main goal of our study was to investigate the antidepressant activity of Formulated Sertraline hydrochloride-loaded Solid Lipid Nanoparticles (SLNPs) by using a rat forced swimming test (FST) and tail suspension test (TST).
Materials and Methods: Animals were divided into three groups, consisting of six rats in each group. Out of these, one group served as control that received distilled water, second group was standard received Sertraline HCl (20 mg/kg intranasal) and third group was received test formulation (SLNPs 50 mg/kg intranasal). To assess the effect of SLNPs on immobility activity through FST and TST were used to take as a measure of antidepressant activity.
Results: SLNPs reduced the immobility duration in TST as well as in FST. In both methods, there was a statistical significant decrease in immobility of SLNPs group when compared to the control group.
Conclusion: The results suggested that SLNPs produced significant antidepressant effect in rats which was comparable with control group and standard Sertraline HCl group animals.

Keywords: Antidepressant activity; sertraline HCl; solid lipid nanoparticles (SLNPs); FST; TST.

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1. INTRODUCTION

Depression is a life-threatening psychiatric disorder and a major public health concern worldwide with an incidence of 5% and lifetime prevalence of 15-20%. Moreover, it is estimated that by 2021 depression will be in the top three contributors to the burden of disease [1,2]. Depression is associated with disability, decreased quality of life, increased health-related costs and is considered main risk factor for many diseases, including cardiovascular, metabolic and neuropsychiatric disorders [3,4]. Current pharmaco-therapeutic treatments have limited efficacy and are associated with many deleterious side effects [5,6]. Therefore, the development of innovative and improved treatments remains crucial. Hence, animal models are essential for advance research in this field. In this view, the present study was designed to preclinical screening the ability of SLNPs as antidepressants in rats.

2. MATERIALS AND METHODS

2.1 Chemicals and Reagents

Sertraline HCl was obtained from Wockhardt, Aurangabad, India.

2.2 SLNPs Preparation

The hot homogenization method was used for the preparation of sertraline hydrochloride-loaded SLNs [7].

2.3 Animals

The experiments were performed on healthy albino Wistar rats (150-220 g) of both sex that were procured from Laxmi Biofarms Pvt Ltd, Pune. The animals were freely accessible to water and foods, and further acclimatized for at least one week before use. The rat experiment was approved by the IAEC (approval ref no.1554/PO/Re/S/11/ CPCSEA).

2.4 Tail Suspension Test

Tail suspension induced immobility that was measured According to Steru et al. [8]. Rats (150-220g) were randomly divided into three groups (n=6).

Group I: Group control given Distilled water.

Group II: Standard Group animals received Sertraline HCL (20 mg/kg) by nasal route

Group III: Test Group animals received SLNPs-(50 mg/kg) by nasal route

All the drugs were given 1 hour before the experiment.

Tail suspension test was performed by suspending the rat by its tail using adhesive tape placed ~1cm from tip of the tail thereby holding it 50 cm above the ground. The immobility time, was recorded on the basis of absence of escape behavior, in each rat for 6 mins.

2.5 Forced Swimming Test

The Forced Swim test (FST) was performed according to the method described by Porsolt et al. [9]. Forced swim test was performed in a glass cylinder (21 × 21 × 50 cm) filled with water up to 35 cm and maintained at 24 ± 1˚C. Individual rat had undergone pretest by placing them in cylinder for 15 mins and later at room temperature. On the next day, each rat was placed again in the cylinder for 6 mins under the same conditions and immobility time was measured. Immobility was marked by the absence of movement to escape and float in water or making efforts other than those to keep its head above water level. To avoid any behavioral changes, due to contamination, water was changed frequently, and after the test period of 6 mins, animals were dried with help of drying paper.

Immobility time for 4 min and 6 mins were recorded. After 2 mins of vigorous activity, every one animal implicated immobile posture. The overall duration of immobility was determined and accordingly graded. The reduction in immobility duration was used as antidepressant activity for all the groups.

2.6 Statistical Analysis

Results were articulated in terms of mean ± SEM (n=6), with use of statistical analysis by one way ANOVA along with Turkey-Kramer test by using Graph Pad Instat Software. p- values less than 0.05 was considered to be statistically significant ($P<0.05$).

3. RESULTS

3.1 Tail Suspension Test

Administered standard Sertraline HCL (20 mg/kg, Intranasal) produced significantly (P<0.01) reduction in the duration of immobility (72.5±7.22) in rats as compared to the control group animals. The SLNPs at doses of 50 mg/kg by nasal route significantly (P<0.05) decreased the duration of immobility (77.3±12.04).

3.2 Forced Swimming Test

There was a statistically significant (P<0.05) decrease in the immobility in standard and test group when compared to the control group. Administered Standard Sertraline HCL (20 mg/kg, Intranasal) exhibited significant (P<0.05) decrease in the Immobility period to 48.83±1.96.The SLNPs at doses of 50 mg/kg intranasal showed significant (P<0.05) decrease in duration of immobility to 46.3±2.376.

4. DISCUSSION

Depression is a type of mood illness characterized by a continuous sense of sadness and a loss of interest. It affects behavioral characteristics which lead to mental and physical difficulties. It's also known as major depressive disorder or clinical depression [10]. Depression occurs due to deficiency in the biogenic monoamine such as serotonin (5HT), dopamine (DA) and noradrenaline (NA) [11]. The treatment with antidepressants was done on the basis of their ability to improve monoaminergic transmission. The screening models help to find the efficacy of SLNPs with respect to a standard drug [12].

SLNPs are made up of biocompatible, biodegradable, non-toxic lipids and they are small in particle size and lipophilic nature. So, SLNs have an innate ability to traverse the Blood brain barrier, making them a suitable carrier for medication delivery into the brain [13].

The major finding of this study revealed that Solid Lipid Nanoparticles-F6 (SLNPs-F6) have antidepressant effects in FST and TST depression models. In both FST and TST, solid lipid nanoparticles - F6 (50mg/kg) reduced the immobility duration [Fig. 1] [11].

Forced swimming test (FST) and tail suspension tests (TST) act as the behavioral despair model, claim to mimic a condition like to that of human depression. The experiments were based on the finding that when animals were placed in an inescapable chamber, they establish an immobile posture after making initial escape-oriented movements. The immobility was assumed to be due to either a lack of consistency in escape-directed behavior or a lack of motivation (i.e. behavioral despair) or the emergence of passive behavior that prevents the animal from engaging in active means of coping with stressful circumstances.

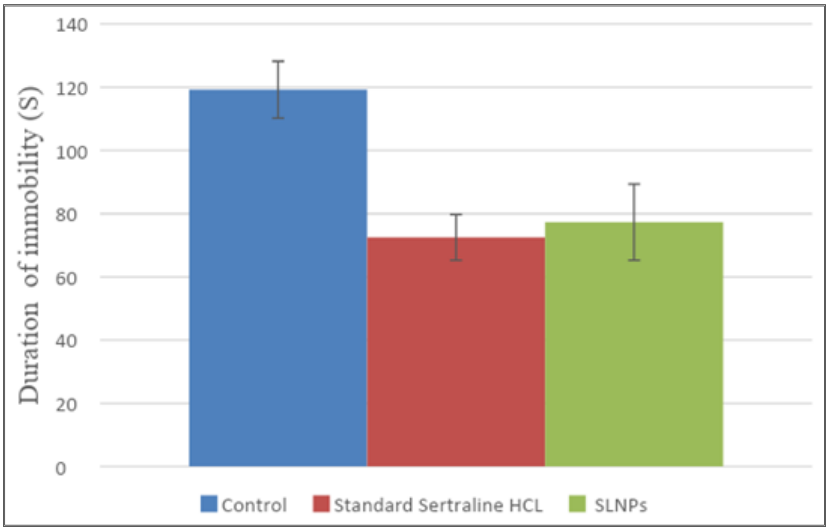

Fig. 1. Effect of SLNPs on the duration of immobility (s) in the rat of tail suspension test

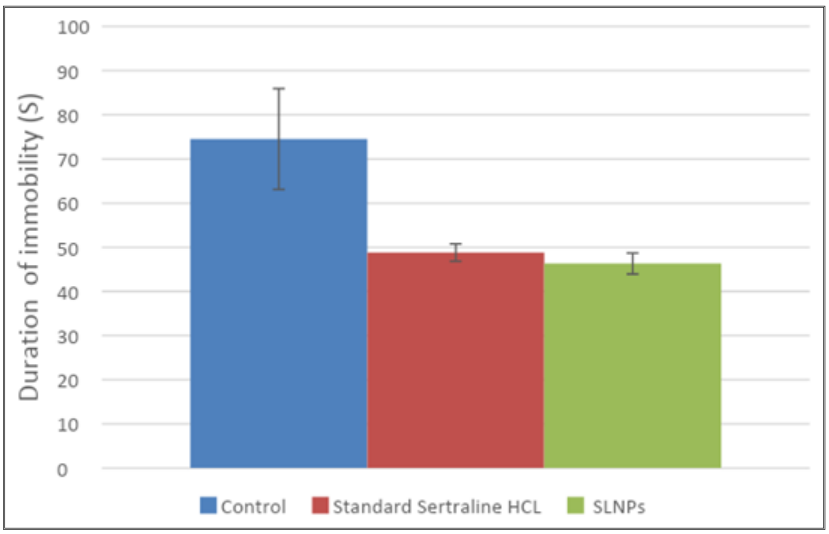

Fig. 2. Effect of SLNPs on the duration of immobility (s) in the rat of forced swimming test

In the FST and TST, pre-treatment with SLNPs-F6 (50 mg/kg) and Sertraline HCL (20 mg/kg) significantly reduced immobility time [Figs. 1 & 2]. The attenuating effect of SLNPs-F6 on endogenous depression may be explained to escape-directed behaviors with minimal immobility posture shown by SLNPs-F6 treated rats. TST reveals anti-immobility effects from a wide range of antidepressants, including tricyclic antidepressants (TCA), electro-convulsive shock (ECS), monoamine oxidase inhibitors (MAOI), selective serotonin uptake inhibitors (SSRI), and even atypical antidepressants. As a result, SLNPs-activity F6's could be interpreted by anyone established mechanism [11].

The forced swimming test in rodents thus is a well-known behavioral test that predicts the clinical efficacy of various types of antidepressants and explores the mechanism of action [14]. Monoamines (5-HT, noradrenaline, and dopamine) play a critical role in the development of the depression syndrome [11]. The FST stress dramatically enhanced MAO-A and MAO-B activity, lowering neurotransmitter levels in the mouse brain, according to the findings. MAO-A decreased neurotransmitters like 5-HT and NE particularly, while MAO-A and MAO-B jointly decreased DA [12]. Depression is thought to be a condition caused by malfunctions in neurotransmitters such as serotonin, dopamine, and noradrenaline [15].

5. CONCLUSION

The present study has shown antidepressant activity of SLNP-F6 in all classic models such as forced swimming test (FST) and tail suspension test (TST) comparable to the control group animals and standard drug Sertraline hydrochloride. However, further studies are needed to elicit its exact mechanism of action and to identify the active ingredient as a potent and effective antidepressant agent.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The experimental protocol was approved by the Institutional Animal Ethical Committee (approval ref no.1554/PO/Re/S/11/CPCSEA).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Levinson DF. The genetics of depression: a review. Biol. Psychiatry. 2006;60:84-92.
2. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet. 1997;349:1498-1504.
3. Cryan J F, Holmes A. The ascent of mouse: advances in modelling human depression and anxiety. Nature Reviews. Drug Discov. 2005;4:775-790.
4. Thase M E. Managing depressive and anxiety disorders with escitalopram. Expert Opin Pharmacother. 2006;7:429-440.
5. Lam R W, Kennedy S H. Evidence-based strategies for achieving and sustaining full remission in depression: Focus on metaanalyses. Can. Psychiatr Assoc. J. 2004;49:17S-26S.
6. Dording CM, Mischoulon D, Petersen TJ, Kornbluh R. The pharmacologic management of SSRI-induced side effects: a survey of psychiatrists. Ann Clin Psychiatry. 2002;14(3):143-7.
7. Hangargekar SR, Mohanty PK, Jain A. Formulation and evaluation of solid lipid nanoparticles of sertraline hydrochloride. Int. J. Pharm. Sci. Drug Res. 2021;13(2): 152-157.
8. Steru L, Chermat R, Thierry B, Simon P. The tail suspension test: A new method for screening antidepressants in mice. Psychopharmacol. 1985;85:367–70.
9. Porsolt RD, Bertin A, Jalfre M. Behavioral despair in mice: A primary screening test for antidepressants. Arch Int Pharmacodyn Ther. 1977;229:327-36.
10. Kanter JW, Busch AM, Weeks CE, Landes SJ. The nature of clinical depression: symptoms, syndromes, and behavior analysis. Behav Anal. 2008;31(1): 1-21.
11. Bhattamisra SK, Khanna VK, Agrawal AK, Singh PN, Singh SK. Antidepressant activity of standardised extract of *Marsilea minuta* Linn. J Ethnopharmacol. 2008; 117(1):51-7.
12. Rasool A, Zulfajri M, Hanafiah M. Evaluation of antidepressant activity of methanolic and hydroalcoholic extracts of *Acorus calamus* L. rhizome through tail suspension test and forced swimming test of mice. J. Tradit. Chin. Med. Sci. 2020;7: 301-307.
13. Rana I, Khan N, Ansari MM, Shah FA, Din Fu, Sarwar S. Solid lipid nanoparticles-mediated enhanced antidepressant activity of duloxetine in lipopolysaccharide-induced depressive model. Colloids and Surfaces B: Biointerfaces. 2020;194:111209.
14. Foyet HS, Tsala DE, Ngatanko AHH. Enhancing Spatial Memory: Anxiolytic and Antidepressant Effects of Tapinanthus dodoneifolius (DC) Danser in Mice. Neurol. Res. Int. 2014;974308.
15. Shoeb A, Chowta M, Pallempati G, Rai A, Singh A. Evaluation of antidepressant activity of vanillin in mice. Indian J Pharmacol. 2013;45(2):141-144.

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