



# A REVIEW ARTICLE ON SUSTAINED RELEASE TABLET OF VENLAFAXINE HYDROCHLORIDE AN ANTIDEPRESSANT DRUG

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## ABSTRACT

The main objective and aim of the presenting review article is to provide information about drug Venlafaxine Hydrochloride as an Antidepressant drug. And how we can manufacture sustained release tablet of it. Oral route is most conventional for route of administration to obtain rapid and complete systemic drug absorption and onset of action. That's why we preferred oral route. This review article involves the venlafaxine hydrochloride drug profile, need of development of sustained release tablet, excipient used in sustained-release tablet and different techniques used to manufacturing, and evaluation parameters.

**Keywords:** Venlafaxine Hydrochloride, Sustained Release Tablet, Manufacturing Technique for Sustained Release Tablet, Evaluation Parameter of Sustained Release Tablet.

## INTRODUCTION

Depression is a major depressive disorder. Globally it is estimated that 5% of adults suffer from depression. People aged 12-25 have the highest rate of depression. Venlafaxine hydrochloride belongs to the class SNRI (Selective serotonin and norepinephrine reuptake inhibitor). It is used for other depressive disorders too like anxiety.

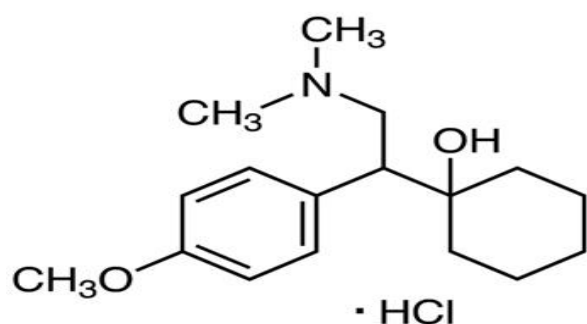
### Venlafaxine Hydrochloride-

The antidepressant venlafaxine HCl belongs to the SNRI class. Wyeth's initial introduction came in 1993. Within 3 days of oral multiple dosage therapy, venlafaxine and o-desmethyl venlafaxine steady-state plasma concentrations are reached. Over the 75 to 450 mg/day dosing range, these concentrations showed linear kinetics. Venlafaxine is a member of the SNRI class. SNRIs are a group of drugs that effectively alleviate chronic pain.

SNRI reduce depression by altering the neurotransmitters that allow brain cells to communicate. In BCS class 1, venlafaxine HCl is classified. being both very soluble and permeable.

## 1. DRUG PROFILE

1. **Drug name:** venlafaxine hydrochloride
2. **Molecular weight:** 313 g/mole
3. **Molecular formula:**  $C_{17}H_{27}NO_2.HCl$
4. **Molecular structure:**



5. **Chemical name:**  
1-[2-(dimethylamino)-1-(4 methophenyl) ethyl] cyclohexane.

6. **Physicochemical properties:**

- **Appearance-** white crystalline powder
- **Solubility:** Slightly soluble in ethanol and methanol, and freely soluble in water.
- **Melting point:** 215-217°C

7. **Pharmacokinetics profile:**

- **BCS class:** class I
- **Half Life:** 4.5 to 5.5 hrs.
- **Bioavailability** - 42±15 %
- **Protein binding** –  
27±2 parent compound.  
30 ±12 % active metabolites.
- **Therapeutic use-** The neurotransmitter that brain cells utilise to communicate is affected by venlafaxine HCl. It is an effective dual inhibitor of norepinephrine (NE) and serotonin (5-HT) reuptake that is orally active.

## 8. Mechanism of Action:

The mechanism of action of the antidepressant venlafaxine hydrochloride is thought to entail inhibition of the serotonin (5-HT) and norepinephrine uptake pumps with uptake. At larger doses, NE inhibition is particularly relevant. SNRIs treat depression by ultimately causing alterations in the brain's chemistry and communication between circuits known to control mood. Serotonin levels are raised with SNRI drugs. additionally norepinephrine in the brain.

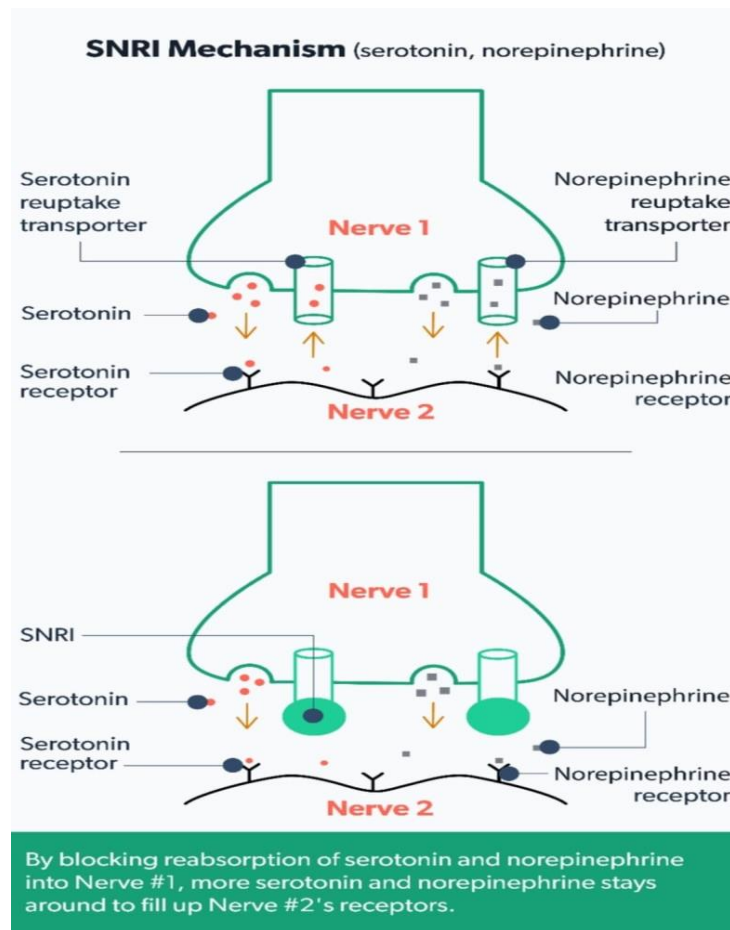


Fig.1. Mechanism of SNRI class

## 9. Pharmacokinetics:

- **Absorption-** Venlafaxine hydrochloride orally administered it rapidly get absorbed from GIT
- **Distribution:** 30±12 active metabolites and 272 parent compounds bind to proteins.
- **Metabolism:** The liver processes venlafaxine HCL extensively and absorbs it efficiently.
- **Excretion:** Thus, the primary route of excretion for venlafaxine and its metabolites is renal elimination.

## 2. ADVANTAGE OF SUSTAINED RELEASE TABLET

- Allow for the maintenance of a body's drug level. Constant
- Reduce the possibility of drug burst relearning
- Increase patient compliance, especially for long-term conditions.
- Zero order delivery is feasible, and the release rate depends on the type of polymer.
- Less medication is administered frequently.
- More practical.

It is possible to better control drug absorption and maximise availability with a little dose.

- Increase treatment effectiveness.
- Delivers API to target site directly.

### 3. NEED OF DEVELOPMENT OF SUSTAINED RELEASE TABLET

- Use fewer dosage tabs with sustained release.

The SR tablet gradually dissolves. They accomplish this by releasing tiny amounts into the patient's system over time.

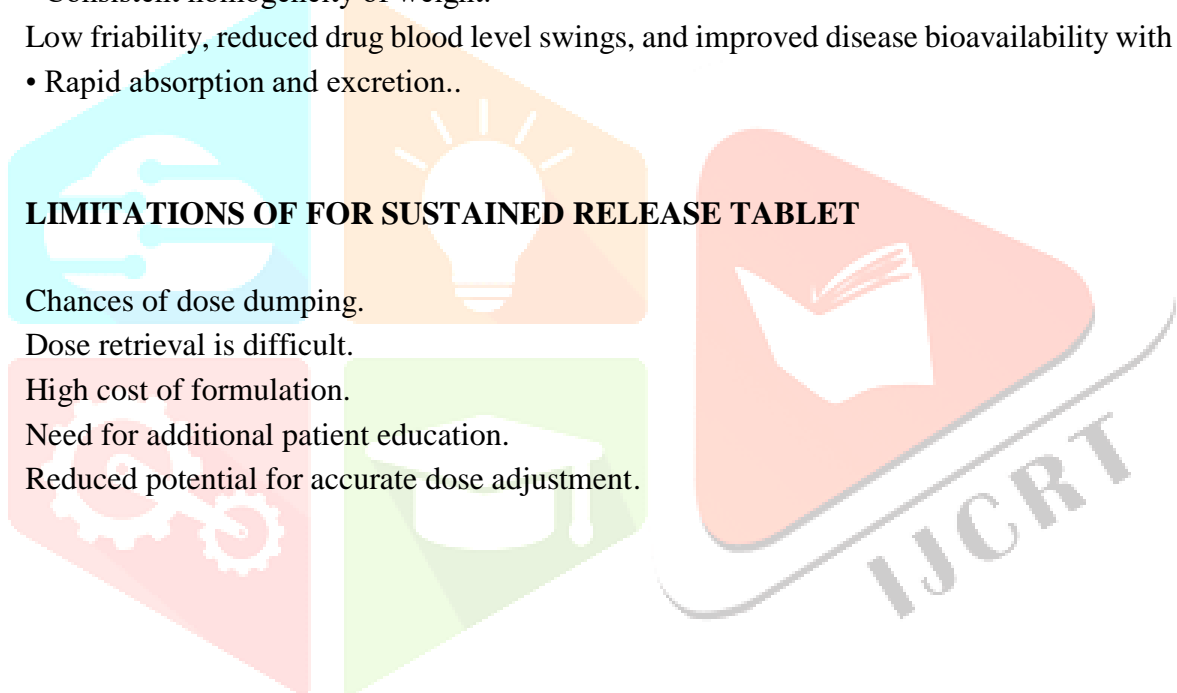
- By constantly delivering the medicine, it produces long-lasting therapeutic effects.
- Continue the effort.

### CHARACTERISTICS OF SUSTAINED RELEASE TABLET

- Even thickness.
- Consistent homogeneity of weight.
- Low friability, reduced drug blood level swings, and improved disease bioavailability with a low dose.
- Rapid absorption and excretion..

### 4. LIMITATIONS OF FOR SUSTAINED RELEASE TABLET

- Chances of dose dumping.
- Dose retrieval is difficult.
- High cost of formulation.
- Need for additional patient education.
- Reduced potential for accurate dose adjustment.



## 5. INGREDIENTS USED IN SUSTAINED RELEASE TABLET

Table no.1: List of ingredient

Hydroxypopyl methylcellulose K4M	Polymer
Hydroxypopyl methylcellulose K 15	Polymer
Hydroxypopyl methylcellulose K 100	Polymer
Carbopol 934	Synthetic polymer, Absorb water.
Xanthum gum	Polymer, Stabilizing agent
Microcrystalline cellulose (MCC)	Anti-cacking Bulking agent
Mannitol	Diuretic
Dicalcium phosphate (DCP)	Buffering, Stabilizer
Talc	Glidant
Magnesium stearate	Lubricant
Eudragit	Polymer, Taste masking, Prevent drug release in saliva. Permeable polymer
Ethyl cellulose	Binder Flavouring Fixative Filler
Sodium carboxymethyl cellulose (SCMC)	Flocculating agent, Thickening agent, Water retaining.

## 6. DIFFERENT TECHNIQUES THAT ARE USED TO MANUFACTURED IN SR TABLET:

Table no.2: techniques used in tablet

Techniques	Procedure
Dry granulation	Dry granulation uses mechanical compression(slugs) or compaction(roller compaction) to facilitate the agglomeration of dry powder particles.
Wet granulation	Wet granulation uses granulation liquid(binder/solvent) to facilitate the agglomeration by formation of wet mass by adhesion.
Direct compression	Direct compression process consists of three steps: raw material, blending, tableting, and coating.

## 7. EVALUATION PARAMETERS FOR SUSTAINED RELEASE TABLET AS PER IP

Here we classify the tests/ parameters by pre-compression parameters and post-compression parameter.

### A. Pre-compression tests:

We have to prepare the mixture of API and excipients to form homogeneous powder, so these tests are performed for the powder before compression.

#### 1. Angle of repose

The purpose of measuring the angle of repose is to ascertain both the flow characteristics of powder and the level of interparticle friction. In this experiment, we measured the height of the pile and the radius of the pile generated using the fixed-height funnel method.

**Formula for calculation:**

$$\tan \theta = h/r$$

Table no.3

Angle of repose	Flow ability
25-30	Excellent flow
31-35	Good flow
36-40	Fair
41-45	Passable
46-55	Poor flow/ cohesive
56-66	Very poor flow
>66	Approximately no flow

#### 2. Car's index and Hausner's ratio:

For the purpose of determining the compressibility factor, these two experiments are conducted. We must determine the bulk density and tapped density for these two ratios.

Formula for calculation:

$$\text{Car's index} = \frac{V^0 - V^f}{V^0} \quad \text{Hausner's ratio: } \frac{V^0}{V^f}$$

Table no.4

Limits	Car's index	Hausner's ratio
Excellent	0-10	1.1-1.11
Good	10-15	1.12-1.18
Fair	16-20	1.19-1.25
Passable	21-25	1.26-1.34
Poor	26-31	1.35-1.45

## B. Post- compression tests

### 1. Physical appearance:

- i.Colour
- ii.Odour
- iii.Taste
- iv.Texture
- v.Breaking line
- vi.Shape

### 2. Weight variation:

The calibration of an electronic balance was used to perform the test weight fluctuation. Take 20 tablets at random from each batch, then weigh each tablet individually. Next, take. Determine the average weight. Comparing a person's weight to the average.

Weight variation given as a percentage of variance.

Table no.5 Weight variation and accepted as per I.P.

Average weight of tablet	Percentage of deviation
80mg or less than 80mg	10.0±2 %
More than 80mg but less than 250mg	7.5±2%
250mg or more than 250mg	5.0±2%

### 3. Hardness:

The "crushing strength" of a tablet is its hardness. The force needed to break the tablet depends on its hardness. compression that is directed diagonally ten pills were tested using the Monsanto, Pfizer, Erweka, and Schleuniger hardness testers.

Table no.6

Tablet type	Hardness
Oral	4kg-10kg
Hypodermic and chewable tablet	3kg
Sustained release tablet	4kg-7.5kg

### 4. Friability:

The stage of being floppy. the likelihood or propensity for a tablet's solid components to fragment when rubbed. The friabilator device is used to conduct this test. 20 tablets were randomly tested in a lab friability testing for 4 minutes and 25 revolutions.

**Formula for calculation:**

$$\% \text{ Of friability} = \frac{\text{initial weight} - \text{final weight}}{\text{initial weight}} \times 100$$

Limit of friability is **not more than 1.0 %**.

5.

**Dissolution study:**

The USP type II (Paddle apparatus) device is used to measure the rate of sustained release tablet dissolution. We must prepare a dissolution medium of phosphate buffer 6.8 pH and 0.1 N HCl for this test. Set the rotation speed in 900 ml to 50 rpm and the temperature to 37°C. After a predetermined amount of time, the dissolution media must be filtered and removed. And a UV-visible spectrophotometer at its maximum wavelength was used to check the filtered solution. Calculate the cumulative percent of medication release as well.

**Drug release kinetics:**

Mathematical models for drug release study

**i. Zero Order Model**

It is ideal way to improve therapeutic effect and avoid side effect of drug. Here drug release rate independent on concentration.

**Equation:**

$$Q_t = Q_0 + K_0 t$$

$Q_0$  = initial amount of drug.

$Q_t$  = cumulative amount of drug release at time (t)

$K_0$  = zero order release constant

t = time in hours

Graphical representation = % CDR v/s Time.

**ii. First Order Model**

First order is occurred when a constant proportion of the drug is eliminated per unit time.

$$Q_t = Q_0 e^{-kt}$$

$Q_0$  = initial amount of drug.

$Q_t$  = cumulative amount of drug release at time (t)

$k$  = first order release constant

t = time in hours

Graphical representation = % CDR v/s Time



### iii. Higuchi Model

The Higuchi model was originally conceived to describe the release of a drug.

$$Q = k_H t^{1/2}$$

$Q$  = cumulative amount of drug release at time ( $t$ )

$k_H$  = higuchi constant

$t$  = time in hours

Graphical representation = amount of drug release v/s square root of time in hrs.

### iv. Korsmeyer – Peppas model

This model of drug release is simply known as “**power law**” describing drug release.

$$F = (M_t/M) = K_m t^n$$

$F$  = fraction of drug released at time  $t$

$M_t$  = amount of drug release at  $t$

$M$  = total amount of drug in dosage form

$K_m$  = kinetic constant

$n$  = diffusion or release exponent

$t$  = time in hrs.

Graphical representation = log % of drug release v/s log time in hrs

### 8. Hydrochloride:

- |     |                       |
|-----|-----------------------|
| 1)  | Venish SR 37.5/75/150 |
| 2)  | Venzee XR 37.5        |
| 3)  | Venlavin SR 37.5      |
| 4)  | Effexor XR            |
| 5)  | Velfex 37.5           |
| 6)  | Venzee XR 150         |
| 7)  | Velax SR 75           |
| 8)  | Verivan ER 37.5       |
| 9)  | Vendas XR 75          |
| 10) | Psyfax 37.5 ER        |
| 11) | Ventab XL 37.5        |
| 12) | Venlift OD 150        |
| 13) | Ventab XL 150         |

### Marketed formulation of Venlafaxine

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