



# FORMULATION AND EVALUATION OF NATURAL POLYMER BASED SUSTAINED RELEASE MICROSPHERES

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## ABSTRACT

The purposed study was to attempt the preparation of sustained released microspheres with the natural polymers. The main obstacle in the preparation of the microsphere was the swelling ability and solubility of the banana flour that the microspheres. This restricts the preparation of microspheres of Venlafaxine HCl by simple techniques of double emulsion technique. In the present study the sustained release microspheres were attempted to prepare with Banana flour as a main natural polymer and xanthan gum, gaur gum as a co-polymer. The ionic gelation technique was used to prepare sustained release microspheres with Venlafaxine HCl. The prepared microspheres were characterized for scanning electron microscopy and micromeritic properties. Other studies like drug content, drug entrapment efficiency and drug release studies were also carried out. The resulting microspheres of batch V4 were found to be shown good at drug content, drug entrapment efficiency and also the drug release studies which was found to be 97.08%. From this study we can conclude that the microspheres can be prepared using banana powder as a natural polymer.

**Index Terms – Sustained Drug Delivery, Microspheres, Banana Flour, Venlafaxine HCL, Ionic gelation technique.**

## INTRODUCTION

The goal of controlled release medication delivery systems is to maximize therapeutic efficacy and bioavailability while minimizing local and systemic negative effects. Since no organic solvents are used in the formulation, ionotropic gelation is one of the most environmentally benign methods for encapsulating the required medicine. When cross-linked by different methods, naturally occurring polysaccharides have demonstrated a considerable potential for several pharmaceutical applications, including the construction of controlled release drug delivery systems. Banana flour i.e., *Musa paradisiaca L.* characterized by the presence of starches and acids shortages that makes it a highly sensitive product to oxygen as well as heat. Prebiotic, Weight loss, Increase absorption and capacity of antioxidants and minerals, reduce blood pressure, modify the metabolism and improve the immune system. Preliminary studies have shown that increased resistant starch may reduce risk of obesity, colon cancer and diabetes. This resistant starch is a type of starch that the stomach cannot easily digest, so it eases the passage of food.

The drug of choice for the present study is a water-soluble drug which is Venlafaxine HCl. Venlafaxine is used to treat depression. It may improve your mood and energy level, and may help restore your interest in daily living. Venlafaxine is known as a serotonin-norepinephrine reuptake inhibitor (SNRI). It works by helping to restore the balance of certain natural substances (serotonin and norepinephrine) in the brain. According to the biopharmaceutics classification systems VNL HCl can be assigned to BCS class I. It is administered typically orally as a tablet having half-life of 4 hours.

The controlled release/sustained release dose formulations have proven incredibly popular. These cutting-edge controlled release approaches quickly replace the standard dose formulations. Drug delivery systems that are intended to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose are referred to as sustained-release, prolonged-release, modified release, extended-release, or depot formulations. The simplest definition of sustained-release is “Any drug or dosage form or prescription that prolongs the therapeutic activity of drug.” The main goal is for the drug to be released into the body at a predetermined pace for the specified duration once the drug-carrier material has been injected, otherwise implanted, or taken orally.

In the present study, microspheres were prepared by encapsulating banana flour with xanthan gum, guar gum respectively with sodium alginate by ionic gelation technique with an aim to prepare and improve its delivery characteristics.

## MATERIALS AND METHODS

### Materials

Raw Banana flour was purchased from southern health foods ltd, Venlafaxine HCl was obtained as a gift sample from IPCA Laboratories, Mumbai. Xanthan gum, guar gum, Sodium alginate, CaCl<sub>2</sub> used were of analytical grade.

### Methods

#### Preparation of Venlafaxine HCL loaded microspheres

The microspheres of Venlafaxine HCl were prepared by using an ionic gelation technique. The polymers used in the formulation were sodium alginate, Banana powder and gums. The polymeric solution was prepared by dissolving sodium alginate and gums in 10 ml of distilled water and sonicated for 20 min to remove air bubbles. The drug was dissolved in distilled water. The prepared polymer solution was added dropwise through a 26-gauge hypodermic needle into a 50 ml of 10 % w/v of calcium chloride solution which is used as cross-linking agents, with stirring at 600 rpm. The prepared microsphere was allowed to stir with the cross-linking agent for one hour. The prepared microspheres were filtered and washed 2-3 times with distilled water to remove the traces of calcium chloride solution. The microsphere was then dried at room temperature for 12 hrs.

**Table no. 1 : Formulation of Microspheres of Venlafaxine HCl By Ionic Gelation Method**

Formulation Code	Venlafaxine HCl (mg)	Sodium Alginate (mg)	Xanthan Gum (mg)	Guar Gum (mg)	Banana Powder (mg)	Distilled Water (ml)	Calcium Chloride (%)
V1	100	75	75	-	20	10	10%
V2	100	100	100	-	30	10	10%
V3	100	75	-	75	20	10	10%
V4	100	100	-	100	30	10	10%



**Fig no.1: Prepared microspheres before drying**

## Evaluation of Microspheres

After drying, the microspheres created using the aforementioned procedure were weighed and their SEM, and micromeritic characteristics were assessed. Studies on the drug content, drug entrapment effectiveness, and drug release were also conducted.

### Scanning Electron Microscopy

Scanning electron microscopy has been used to determine particle size distribution, and texture and to examine the morphology of the fractured or sectioned surface.



Fig no.2 : SEM photograph of optimized batch V4 of venlafaxine HCl

### Percentage Yield

The yield of the prepared formulations was calculated as the percentage of the weight of the dried product at room temperature compared to the theoretical amount. Product yield is calculated by using the following Equation,

$$\text{Product Yield} = \frac{\text{Weight of The Product}}{\text{Weight of Raw Materials}} \times 100$$

### Micromeritic Studies

The prepared microspheres are characterised by their micromeritics properties such as bulk density, tapped density, Carr's compressibility index, Hauser's ratio and angle of repose.

#### The Bulk density

The bulk density is defined as the mass of powder divided by the bulk volume. Bulk density was measured by pouring the pre-weight microspheres into a graduated cylinder. The bulk volume ( $V_b$ ) of the blend was determined. The bulk density was calculated by dividing the weight of the samples in grams by the bulk volume in  $\text{cm}^3$ . The bulk density was calculated by using the following formula,

$$\text{Bulk density} = \frac{\text{Mass of Microspheres}}{\text{Volume of Microspheres Before Tapping}}$$

## Tapped Density

Tapped density is the volume of powder determined by tapping by using a measuring cylinder containing a known mass of microsphere that were tapped for a next fixed time, and the minimum volume occupied in the cylinder was measured. The tapped density was calculated by using the following formula,

$$\text{Tapped Density} = \text{Volume of Microspheres} / \text{Volume of Microspheres After Tapping}$$

## Carr's Compressibility Index

It is a technique for figuring out flow characteristics and is also known as the percent consolidation index. It is directly correlated with the particle size, cohesiveness, and relative flow rate. It is a straightforward, quick, and well-liked method of forecasting powder flow characteristics. This characteristic is crucial for maintaining weight uniformity. The formula used to compute it is,

$$\% \text{ Compressibility Index} = \text{Tapped Density} - \text{Bulk Density} / \text{Tapped Density} \times 100$$

## Hausner's Ratio

A similar index like percentage compressibility index has been defined by Hausner's. Values less than 1.25 indicate good flow, where as greater than 1.25 indicates poor flow. Added glidant normally improve flow of the material under study. Hausner's ratio can be calculated by formula,

$$\text{Hausner's Ratio} = \text{Tapped Density} / \text{Bulk Density} \times 100$$

## Angle of Repose

Any pharmaceutical tablet, capsule, or powder formulation needs to have good flow characteristics. In order to swiftly identify an ideal formulation, it is crucial to accurately measure flow attributes as early in the development process as possible. The angle of repose is used to assess the interparticle interactions between particles as well as the flow properties of powders. The greatest angle that can be formed between the surface and horizontal plane is known as the angle of repose. The glass funnel method was used to calculate the angle of repose of each powder mixture. The microspheres formed a heap after being precisely weighed and flowing freely down the funnel. The funnel's height was modified such that its tip just touched the top of the mound. The powder cone's diameter was measured, and the angle of repose was determined using the equation below.

$$\text{Tan } \theta = h / r$$

Where,  $\theta$  = angle of repose

h = height of pile and

r = radius of the base of surface.

The angle of repose affects particle size distribution, as larger the particle size, it will flow freely and vice-versa. It is a helpful parameter to monitor the quality of powdered or granular pharmaceutical formulations. For good flowing materials, the angle of repose should be less than 30°.

Table no.2 : percentage yield and micromeritic properties of venlafaxine HCl microspheres

Formulation Code	Percent Yield (%)	Bulk Density(g/cc)	Tapped Density(g/cc)	Cars Compressibility (%)	Hausner's Ratio	Angle of Repose (θ)
V1	90.96 %	307	409.33	25 %	1.33	26.56 <sup>0</sup>
V2	93.81 %	258	387	33.33%	1.5	24.70 <sup>0</sup>
V3	88.14 %	158.66	216.36	26.67%	1.36	43.15 <sup>0</sup>
V4	95.72 %	350	450	22.22%	1.28	16.38 <sup>0</sup>

### Drug Content

The prepared formulations were examined for drug content. 10 mg of the prepared formulation was taken on 10 ml of phosphate buffer of pH 6.8. The suspension was sonicated for 10 min to allow the untrapped drug to be dispersed. This suspension is further centrifuged for 15 min at 1600 rpm. The resultant supernatant was decanted and assayed in UV Spectrophotometer and absorbance was taken at 224nm. The residue after drying was assayed in UV for entrapped drug estimation with phosphate buffer 6.8 at 224nm. The drug content was then calculated by using the formula,

$$\text{Total Drug Content} = \text{Untrapped Drug} + \text{Entrapped Drug}$$

### Drug Entrapment Efficiency

The prepared formulations were examined for entrapment efficiency. 10 mg of the prepared formulation was taken in an equivalent quantity of 6.8 phosphate buffer. The suspension is centrifuged at 1600 rpm for 15 minutes.

$$\% \text{ EE} = \text{Actual Drug Content} / \text{Theoretical Drug Content}$$

Table no.3 : drug content and % drug entrapment efficiency

Formulation Code	% Drug Content	Percentage Drug Entrapment
V1	91.27 %	92.37%
V2	87.49 %	89.85 %
V3	97.48 %	95.15 %
V4	95.5 %	96.85 %

### In vitro drug release study

In vitro drug release study was carried out in USP II paddle-type dissolution test apparatus using phosphate buffer pH 6.8 as dissolution medium, Volume of dissolution medium Was 900 ml and bath temperature was maintained at (37±1)°C throughout the study. The stirring speed was adjusted to 100 rpm. At an interval of 1 hour, 10 ml of sample was withdrawn with replacement of 10 ml fresh medium and analysed for Venlafaxine HCl content by UV-Visible spectrophotometer at 224 nm. The cumulative % drug release was calculated and a graph of % cumulative vs. time was plotted.

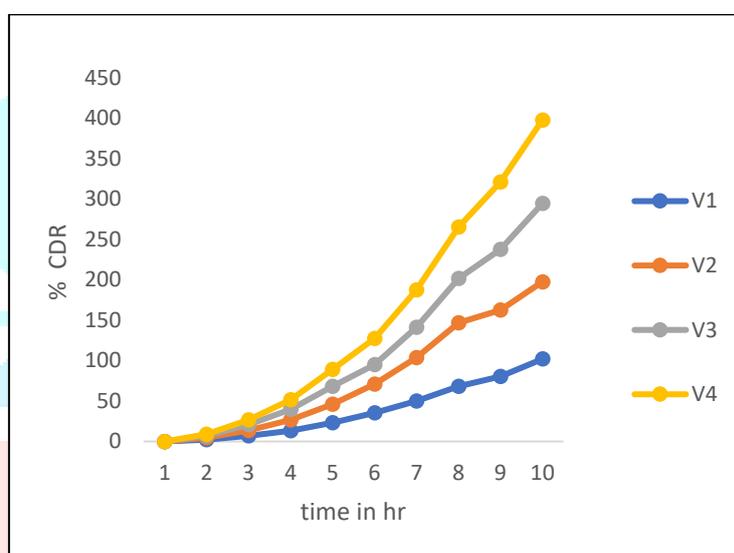
### Details of Dissolution Testing

- ✓ Apparatus: Electrolab USP
- ✓ Dissolution media: Phosphate Buffer 6.8
- ✓ Speed: 100 rpm
- ✓ The volume of medium: 900 ml
- ✓ Aliquots taken at each time interval: 10 ml
- ✓ Temperature: 37 ± 0.5°C

✓ Wavelength: 224 nm

Table no.4 : comparison of % CDR of batches v1, v2, v3, and v4

Time (Hr)	% CDR V1	% CDR V2	% CDR V3	%CDR V4
0	0	0	0	0
1.	2.368252	2.353333	1.99931	2.436228
2.	7.071863	6.808148	5.934094	6.828358
3.	13.48588	13.30741	11.77289	13.09294
4.	23.02789	23.07778	20.65802	22.25882
5.	35.26743	35.64222	32.14522	24.2924
6.	50.13836	53.65852	46.17103	37.52239
7.	68.3325	78.46322	63.40183	54.99152
8.	80.45048	82.31593	83.15009	75.02714
9.	95.0236	93.55296	96.2368	97.08277



Graph : comparison of % CDR of batches v1, v2, v3 and v4

## RESULTS

Microspheres were prepared successfully by the ionic gelation method with banana flour as a natural polymer with sodium alginate and calcium chloride. The percentage yield in all the four batches was found to be greater than 85%. All the formulations have Carr's Index greater than 10 (Table no. 2). The drug content and the drug entrapment efficiency of batch V4 was found to be 95.5 % and 96.85% resp. (Table no. 3). The SEM photograph of the optimised batch V4 Fig no.2 shows that the microspheres prepared were with rough surface. The FTIR of pure drug Venlafaxine is shown in Graph. The prepared microspheres were then evaluated for the drug release rate performance (Table no.3) and the batch V4 showed percent drug release 97.08% which was highest among all the other batches. From this we can conclude that the batch V4 give good results.

## DISCUSSION

The banana flour was used to prepare Venlafaxine HCl microspheres with Ionic gelation method effectively. The  $\text{CaCl}_2$  solution of concentration of 10% was used as the cross-linking agent. The rotation speed of the magnetic stirrer was kept 600 rpm and the polymer solution was dispersed in the  $\text{CaCl}_2$  solution by the 26 G syringe drop by drop. The banana flour was not showing the swelling property or it was not soluble in solvents like water, methanol, acetone. Chloroform etc. To overcome this situation xanthan gum and gaur gum was used with Banana flour as a co-polymer respectively. Xanthan gum and gaur gum helped to encapsulate and engulf the banana flour particles and to prepare microspheres. The batch V4 has shown good results among all other batches hence we can conclude that the microspheres can be prepared effectively with banana powder with ionic gelation technique.

## CONCLUSION

From the above study it may be concluded that the microspheres can be prepared with banana powder as a natural polymer with ionic gelation technique.

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## CONFLICTS OF INTEREST

None

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