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# Formulation, Development and Evaluation of Enteric Coated Tablets of Sodium Valproate by using Wet Granulation Method

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## ABSTRACT

In the present research paper, Sodium valproate tablets were prepared by using Syloid FP244 polymer. The tablets were formulated by using wet granulation techniques. Further post formulation parameters like hardness, friability, weight variations and content uniformity were studied. The results suggested, that the prepared enteric coated tablets specifics all the criteria of the standard formulation as per specified in monographs.

**Keywords:** Sodium valproate, anticonvulsant, enteric coated polymer

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## INTRODUCTION

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The oral route of drug administration is the most popular and successfully used for conventional delivery of drugs. It offers the advantages of convenience, ease of administration, greater flexibility in dosage form design, ease of production, and low cost. The parenteral route of administration is important in case of emergencies, while the topical route of drug administration recently employed to deliver drug to the specific part of the body for systemic effect. It is probable that almost 90% of all the drugs are administered by oral route.

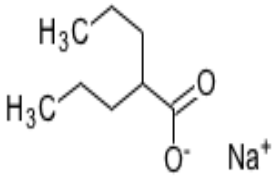


**Figure 1: Chemical Structure of Sodium valproate**

Valproic acid dissociates to the valproate ion in the gastrointestinal tract. It has been suggested that its activity in epilepsy is related to increased brain concentration of gamma-amino butyric acid (GABA). For enteric coated sodium valproate at a dose of 500 mg (valproic acid equivalent 433 mg) twice a day C-max is 91.33 mg/l. The mean T-max value for enteric coated valproate 3.8 h. Valproate is eliminated almost exclusively by hepatic metabolism. The metabolic fate is complex.

## MATERIAL AND METHODS

### Materials

Sodium Valproate was a gift sample provided by Shausan Chemicals and Drugs Limited mumbai. Cellulose Acetate phthalate and Sodium Starch glycolate (Pragti chem. Impact, Mumbai were used as received. All other chemicals used were of analytical grade and were used as received.

**Table 1: Formulation of enteric coated tablets**

| **Ingredients** | **Batch No.** | | | | |
|---|---|---|---|---|---|
| | **D001** (mg) | **D002** (mg) | **D003** (mg) | **D004** (mg) | **D005** (mg) |
| Sodium valproate | 200 | 200 | 200 | 200 | 200 |
| SyloidFP244 | 18 | 20 | 22 | 24 | 226 |
| MCC | 38.5 | 36.5 | 34.5 | 32.5 | 30.5 |
| PVP K-30 | 4.5 | 4.5 | 4.5 | 4.5 | 4.5 |
| Talc | 10.5 | 10.5 | 10.5 | 10.5 | 10.5 |
| Magnesium sterate | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 |
| IPA | q.s | q.s | q.s | q.s | q.s |
| **Total** | 275 | 275 | 275 | 275 | 275 |

### Methods

Preparation of Enteric coated tablets of Sodium Valproate was done by direct compression method using different polimer & disintegrant ratio shown in table 1.

**Procedure for preparation of tablets**

**Dispensing and sifting**

Required quantity of drug and Syloid were weighed, mixed and sifted through 20-mesh sieve. Microcrystalline cellulose and PVP K-30 were weighed and passed through 40-mesh sieve.

**Dry mixing**

After sifting, blend was mixed with other sifted material in rotary mixer.

**Granulation**

The granules were prepared in rapid mix granulator.

**Drying**

Granules were dried at 55-60$^0$C in fluid bed dryer till 0.5 - 1.0 % LOD.

**Sizing**

The granules were milled through oscillating granulator by using 1.2 mm mesh with previously weighed Syloid 244FP.

**Blending and Lubrication**

Blended the dried granules with previously weighed and shifted excipients and Talc 40# in conta blender. Lubrication was done in conta blender with previously weighed and sifted excipients like Talc 40# and Magnesium stearate 40#.

**Compression**

The lubricated blend was directly compressed on rotary machine.

**Seal coating**

Preparation of solid dispersion

1. PVP K-30 was dissolved in half quantity of total IPA
2. Talc was homogenized for 40 minutes in rest quantity of IPA
3. Step I solution was added into Step II dispersion with stirring
4. PEG 400 was added in step III dispersion with stirring

**Enteric coating**

Preparation of coating dispersion

1. CAP was weighed accurately and dissolved in a mixture of ethanol and acetone (1:1)
2. Titanium dioxide homogenized in rest quantity of acetone
3. Step I solution was added in step II dispersion with stirring
4. Dibutyl phthalate was added in step III dispersion with stirring.

**Tablet Evaluation**

Following tests were applied on coated tablet.

**Appearance**

The general appearance and elegance of tablet was identified visually, which include tablet size, shape, color, presence or absence of an odor, surface texture etc.

**Weight variation**

Twenty tablets were weighed individually and average weight was determined. the individual tablet weight was compared with average tablet weight. the coated tablet weight and the maximum percent difference allowed is 5.0%.

**Thickness**

Tablet was selected at random from individual formulations and thickness was measured by using venire caliper scale, which permits accurate measurement. tablet thickness should be controlled within a ± 0.2% variation of standard value.

**Tablet Friability**

Friability is the measure of tablet strength. Roche Friabilator was used for testing the friability using the following procedure. twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min, the tablets were weighed and the percentage loss in tablet weight was determined.

$$\% \text{ Loss } = \frac{\text{Initial wt. of tablet} - \text{Final wt. of tablet}}{\text{Initial wt. of tablet}}$$

**Hardness**

Tablet was selected at random from individual formulations and measured by using Eweka hardness tester.

**Disintegration test**

The disintegration time was measured by using USP disintegration test apparatus. six tablets were placed in tubes and the basket was kept positioned in a 1 litre beaker of 0.1N HCL for two hours followed by 6.8 pH phosphate buffer maintained at $37\pm2^0$C. the tablet remain 2.5 cm from the bottom of medium, a standard motor driven device move the basket containing tablet up and down through a distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minute.

**Dissolution test**

The tablets were evaluated for in vitro drug release was carried out using USP dissolution apparatus. the following conditions were applied.

USP Dissolution apparatus: Type II (Paddle)

Media : 0.1N HCl for two hours followed by 6.8 pH phosphate Buffer

Volume of dissolution media : 1000 mL

Speed of paddle rotation : 100/50 RPM

Temperature : $37^0 \pm 0.5^0$C

Six tablets were subjected to two hours exposure in 0.1N HCL buffer followed by immediate transfer to a dissolution bath containing 6.8 pH phosphate buffer and % drug released was measured. Buffer phase: - Samples were withdrawn from the dissolution vessels at 0, 60, 120, 135, 150, 165, 180 minutes interval. the % drug release was measured U.V method.

## RESULTS AND DISCUSSION

### Evaluation Of Sodium Valporate Tablets

All the formulated batches of Sodium valproate tablets were evaluated according to the specification and following results were obtained. The formulation variables and various Physico-chemical properties of prepared enteric coated tablets are shown in Tables.

### Physical appearance

Tablets showed biconcave, circular shape and white color.

### Thickness

The values were found almost uniform in specific method. Thickness of the tablets in all the formulation batches (D001 to D005) were found in the range from 3.45±0.05 mm to 3.75±0.15 mm.

### Weight variation

The percentage weight variations for all the formulation are tabulated in Table .2. All the tablets passed weight variation test as the % weight variation was within the pharmacopoeia limits of ±7.5%. It was found to be from 287.5 to 293.3 mg. The weight of all the tablets was found to be uniform.

### Hardness

Hardness of the enteric coated tablets was measured using Monsanto tablet hardness tester was shown in Table 5.9. It was found to be from 2.07 to 293.3 kg/cm2.

### Friability

The study results are tabulated in table no.5.10 was found well within the approved range (<1%) in all the formulation batches. the percent friability was determined using the formula. The range of friability was found to be 0.1 to 0.7%.

### Disintegration

Tablets were taken and introduced one tablet in each tube of disintegration apparatus and placed in 1 liter beaker with 6.8 pH buffer and the time of disintegration was recorded. The study was done at room temperature.

**Table 2: Evaluation parameter of enteric coated tablets**

| Batch No. | Wt. Variation | Hardness | Friability | Disintegration |
|---|---|---|---|---|
| D001 | 1.6 | 2.98 | 0.5 | 10-12 |
| D002 | 8.0 | 3.87 | 0.1 | 9-11 |
| D003 | 2.8 | 2.80 | 0.5 | 12-14 |
| D004 | 4.2 | 3.28 | 0.3 | 9-13 |
| D005 | 3.9 | 3.43 | 0.2 | 11-14 |

**In vitro drug release study**

Two hours in 0.1 N Hydrochloric acid, 1000 ml, paddle, 50 rpm, 37°C ± 0.5°C followed by pH 6.8 phosphate buffer, 1000 ml, paddle, 50 rpm, 37°C ± 0.5°C.

**Table 3: Cumulative % drug Release profile**

| Media | Time (min) | % drug released | | | | |
|---|---|---|---|---|---|---|
| | | D001 | D002 | D003 | D004 | D005 |
| **0.1N HCl** | 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | 60 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | 120 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **6.8 pH phosphate buffer** | 135 | 0.1 | 0.1 | 0.1 | 0.0 | 0.2 |
| | 150 | 3.4 | 2.5 | 3.4 | 2.4 | 4.6 |
| | 165 | 9.8 | 7.8 | 9.8 | 7.2 | 7.6 |
| | 180 | 28.8 | 31.7 | 28.8 | 20.0 | 21.2 |
| | 195 | 42.3 | 55.6 | 42.3 | 32.8 | 42.3 |
| | 210 | 53.3 | 60.0 | 53.3 | 63.2 | 50.8 |
| | 225 | 85.7 | 85.2 | 85.7 | 70.5 | 75.1 |
| | 240 | 86.1 | 85.9 | 87.9 | 89.0 | 80.5 |

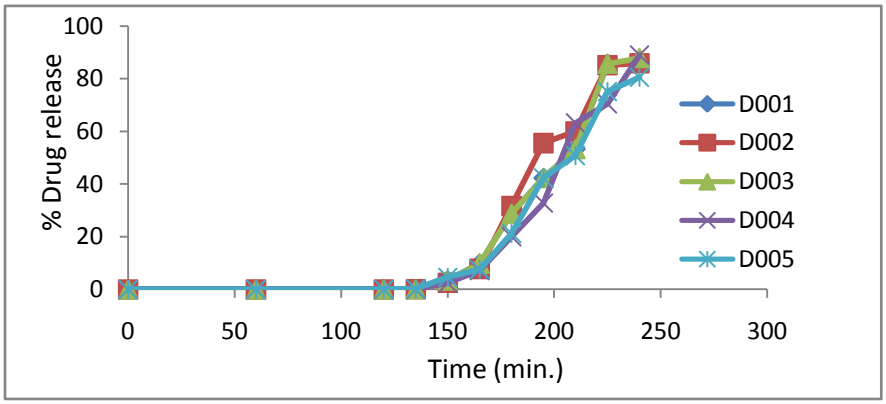


**Figure 2 % cumulative drug release of Sodium valproate tablets.**

## CONCLUSION

From the ongoing studies, it was concluded that, sodium valproate enteric coated tablets

prepared by wet granulation techniques, showed promising results. SyloidFP244 polymer prevents the release of drug for the first 2hrs. The enteric coated tablets are cost effective and exhibit predictable release behavior. Moreover, the hardness, friability and weight variation parameters studies further strengthen the effectiveness of prepared enteric coated formulation.

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