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# Formulation and Evaluation of Allylestrenol Immediate Release Tablets

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## ABSTRACT

Among the different routes of administration, the oral route of administration continues to be the most preferred route due to various advantages including ease of ingestion, avoidance of pain, versatility and most importantly patient compliance. The different dosage forms include tablets and capsules. Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer and lead to better patient compliance. The present work involves the formulation development, optimization and in-vitro evaluation of immediate release allylestrenol tablets. To minimize critical process parameters and since allylestrenol is heat sensitive, direct compression method was selected for the formulation of immediate release allylestrenol tablets. Tablets were prepared using cross carmellose sodium, crosspovidone, pre gelatinized starch and sodium starch glycolate as disintegrants. During the course of study it was found that the formula G4 containing sodium starch glycolate as disintegrant exhibited acceptable disintegration time, percentage drug content per tablet and in vitro drug release. So at last it was concluded that immediate release allylestrenol tablets can be prepared using direct compression which met the required specifications.

**Keywords:** Immediate release tablets; allylestrenol; cross carmellose sodium; crosspovidone; pre gelatinized starch; sodium starch glycolate

## INTRODUCTION

An immediate release dosage form allows a manufacturer to extend market exclusivity, while offering patients a convenient dosage form or dosage regimen.

Immediate release tablets are those tablets which are designed to disintegrate and release their medication with no special rate controlling features, such as special coatings and other techniques [1, 2]. Immediate release and fast dispersing drug delivery system may offer a solution to these problems. Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer, has quick onset of action is economical and lead to better patient compliance. They are also a tool for expanding markets, extending product life cycles and generating opportunities [3, 4].

Allylestrenol also known as allyloestrenol and allyl estrenol, is a synthetic progestogen sometimes used to prevent threatened miscarriage, recurrent pregnancy loss and premature labor [5 6]. In men, it has also been studied as a treatment for benign prostatic hyperplasia, with encouraging results [7 8]. It is chemically (17ß)-17-(prop-2-en-1-yl)estr-4-en-17-ol. A survey of literature has revealed that there is no formulation and evaluation of Allylestrenol tablets.

The plan of present research is to develop a cost effective allylestrenol immediate release tablets by direct compression method. Direct compression is being studied for its simplicity, cost effectiveness and for its comparatively shorter process. Thus five different formulations were designed to obtain best optimized product.

## MATERIALS AND METHODS

### Materials

Allylestrenol was kindly gifted by Renata Ltd, Bangladesh. Acetonitrile of HPLC grade and Methanol of analytical grade were purchased from E. Merck, Darmstadt, Germany. Lactose was obtained from Reliance Ltd., Mumbai, India. Microcrystalline cellulose (Avicel PH 102) and crosscarmellose sodium was purchased from Ashok Chem-Pharma International, Mumbai, India. Magnesium stearate and sodium starch glycolate were purchased from Amishi Drugs & chemicals Private Limited Ahmedabad, India. Pre gelatinized Starch and Crospovidone obtained from Hangzhou Starshine Pharmaceutical Co., Ltd., China, Ludipress was purchased from BASF AG, Ludwigshafen, Germany. Water was deionised and double distilled. All other ingredients used were of analytical grade.

### Preparation of immediate release allylestrenol tablets

Allylestrenol and lactose were accurately weighed, geometrically mixed and passed through #80 mesh and then, microcrystalline cellulose, disintegrants and ludipress were accurately weighed and passed through #20 mesh. Both mixtures were mixed in rapid mixer granulator for 10 minutes as a dry mixing. Then, colloidal anhydrous silica (aerosil 200) and magnesium stearate was passed through #40 mesh ; added to the mixture in the rapid mixer granulator and mixed for 5 minutes. Then the granules were compressed into tablets using 16 stations rotary compressed machine with punch size 6.0 mm.

### Evaluation of immediate release allylestrenol tablets

#### 1. Uniformity of weight

Individually 20 tablets were weighted at random using Sartorious balance (Model CP- 224 S). Average weight was determined. Determinations were made in triplicate.

Limit - Not more than 2 of the individual masses deviate from the average mass by more than the 7.5 % and none deviates by more than 15% [9].

#### 2. Tablet hardness

Automatic Tablet Hardness Tester (8M, Dr. Schleuniger, Switzerland) was used to determine the crushing strength. 6 tablets were randomly selected from each formulation and the pressure at which each tablet crushed was recorded. Determinations were made in triplicate.

Limit - At least 5 kg.

#### 3. Tablet friability

20 tablets of each formulation were weighed and subjected to abrasion by employing a Veego friabilator (VFT-2, India) at 25 rev/min for 4 min. The tablets were then weighed and compared with their initial weights and percentage friability was obtained. Determination was made in triplicate.

Limit - The weight loss should not be more than 1 %.

#### 4. In-vitro disintegration test

6 tablets from each formulation were employed for the test in distilled water at 37°C using Tablet Disintegration Tester (Model: VDT-2, Veego, India). The time required for disintegrating the tablet and passing completely through the sieve was recorded.

Limit - Not more than 30 minutes [10].

**5. Pharmaceutical assay**

The instrument used for the study was HPLC (Agilent) having 1100 series HPLC pump, auto sampler equipped with a 100 µl sample loop, dual absorbance detector, output signal was monitored and integrated using chemstation software on a XTerra® RP18 column (150×4.6 mm, 5µm particle size). Mobile phase was prepared by mixing HPLC grade water and HPLC grade acetonitrile in the ratio of 20:80 v/v. The mobile phase was sonicated for 10 min and filtered through 0.2µm Nylon 6, 6 membrane filter before use. For the preparation of standard stock solution about 20 mg of allylestrenol WS was weighed accurately into a 100 ml volumetric flask and dissolved and diluted to volume with mobile phase to obtain a concentration of 200µg/ml. This stock solution was further diluted to 100 ml with mobile phase to obtain a concentration of 10 µg/ml and filtered through 0.20µm PTFE membrane filter (hydrophilic). For the preparation of sample solution four tablets equivalent to 20 mg of allylestrenol were weighed and transferred into a 100 ml volumetric flask; 60 ml of mobile phase was added and sonicated with occasional shaking for 15 min. The solution was cooled to room temperature and diluted to volume with the mobile phase. The solution was filtered through Whatman Grade 1 Filter Paper. 5 ml of this solution was diluted to 100 ml with mobile phase. The final solution was through 0.20 µm PTFE membrane filter (hydrophilic). The HPLC analysis was performed on reversed-phase high-performance liquid chromatographic system with isocratic elution mode using a mobile phase on X-Terra® RP18 column (150×4.6 mm, 5µm particle size) with 1.5 ml/min flow rate at 205 nm using UV detector. A 100 µl volume of above sample solution and standard solution were injected into HPLC and peak areas were measured under optimized chromatographic conditions.

Limit – 90% to 110% of the label amount

**6. In-vitro dissolution study**

The release rate of allylestrenol from immediate release tablets was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (padodle method). The dissolution test was performed using 500 ml of 1.0 % sodium lauryl sulphate in water, at 37± 0.5 C and 100 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus 5, 10, 20, 30 and 45 minutes. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through a 0.20µm PTFE membrane filter (hydrophilic). A 100 µl volume of above sample solution was injected into HPLC and peak areas were measured under optimized chromatographic conditions as per assay method. Cumulative percentage of drug release was calculated.

Limit - Not less than 75% of labeled amount of allylestrenol was dissolved in 45 min.

## RESULTS AND DISCUSSION

In the present study, various formulations of immediate release allylestrenol tablets were prepared by direct compression. We have chosen to use ludipress because the flow of the material is very good, resulting in the production of tablets with good mechanical resistance and low friability, with an immediate drug release. The use of super disintegrants for preparation of immediate release tablets is highly effective and commercially feasible. These super disintegrants accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking

of tablets and therefore faster disintegration. This disintegration is reported to have an effect on dissolution characteristics as well. Flow properties of the powder, resistance to particle movement can be judged from the angle of repose. Based on angle of repose it was observed that $G_4$ showed excellent flow properties than the rest of formulations. Carr's index of the prepared blends falls in the range of 10.56 to 18.09 % and Hausner factor values were in the range of 1.12 to 1.23. Based on the results obtained we can conclude that $G_4$ showed excellent flow.

Disintegration time is very important for immediate release tablets as it assists swallowing and also plays a role in increasing drug absorption, thus promoting bioavailability. Disintegration time of prepared tablets was within the range (Table 3). In-vitro drug release study on the prepared tablets were done using 0.75% sodium lauryl sulphate in water as medium, at 37± $0.5^0$C from the results it was observed that $G_4$ showed maximum drug release of 93.20% which was higher than other formulations (Table 1).

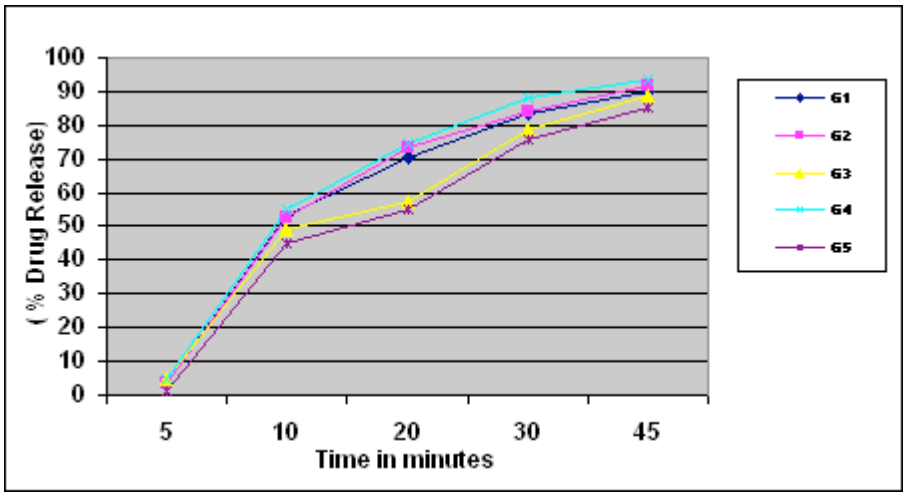
**Table 1: Formulae for Preparation of Immediate Release allylestrenol Tablets**

| SL.NO | INGREDIENTS (mg/tablet) | Batch Code | | | | |
|---|---|---|---|---|---|---|
| | | G1 | G2 | G3 | G4 | G5 |
| 1. | Allylestrenol | 5 mg | 5 mg | 5 mg | 5 mg | 5 mg |
| 2. | Lactose | 20 mg | 20 mg | 20 mg | 20 mg | 20 mg |
| 3. | Ludipress | 49.5 mg | 49.5 mg | 49.5 mg | 49.5 mg | 49.5 mg |
| 4. | Microcrystalline cellulose (Avicel PH 102) | 20 mg | 20 mg | 20 mg | 20 mg | 20 mg |
| 5. | Colloidal anhydrous Silica (Aerosil 200) | 1.5 mg | 1.5 mg | 1.5 mg | 1.5 mg | 1.5 mg |
| 6. | Magnesium Stearate | 1 mg | 1 mg | 1 mg | 1 mg | 1 mg |
| 7. | Croscarmellose sodium | 3 mg | - | - | - | - |
| 8. | Crosspovidone | - | 3 mg | - | - | - |
| 9. | Pre gelatinized Starch | - | - | 3 mg | - | - |
| 10. | Sodium-starch glycolate | - | - | - | 3 mg | - |
| Total weight | | 100 mg | 100 mg | 100 mg | 100 mg | 100 mg |

**Table 2: Dissolution Profile of Formulations**

| Formulation Code | Time in minutes | | | | |
|---|---|---|---|---|---|
| | 5 | 10 | 20 | 30 | 45 |
| G1 | 3.56% | 53.25% | 70.25% | 83.52% | 90.02% |
| G2 | 3.45% | 52.45% | 73.19% | 84.26% | 91.45% |
| G3 | 4.51% | 49.04% | 57.26% | 78.81% | 88.54% |
| G4 | 4.65% | 55.21% | 74.75% | 88.25% | 93.20% |
| G5 | 1.23% | 45.18% | 55.26% | 75.61% | 85.23% |

**Figure 1: Dissolution Profile of Formulations**




## CONCLUSION

Considering some important parameters like disintegration time (2.55 min), percentage drug content per tablet (99.98%), in vitro drug release (93.20%) and cost factor $G_4$ containing Sodium-starch glycolate as disintegrant was selected as the best formulation .It was also observed that
direct compression was the best suitable method used for producing immediate release allylestrenol tablets since it is cost effective and less time consuming. Based on all the above considerations these formulas can be subjected for bio availability studies and if it complies to all the requirement of those studies the same formula can be commercialized.

Table 3-Evaluation of post -compression Parameters

| Formulation Code | Evaluation of post -compression Parameters | | | | | | |
|---|---|---|---|---|---|---|---|
| | Hardness of tablets ($kg/cm^2$) | Friability of tablets (%) | Weight variation (mg) ± % deviation | Percent drug content per tablets (%) | Drug content per tablets (mg) | Thickness of tablets (mm) | Disintegration time (mm) |
| G1 | 7.3 | 0.787 | 95.95 mg ± 1.91% | 99.46 | 4.973 | 3.08 | 3.54 |
| G2 | 7.4 | 0.845 | 96.02 mg ±1.78% | 98.98 | 4.949 | 3.07 | 3.55 |
| G3 | 7.7 | 0.595 | 96.54 mg ±1.15% | 99.86 | 4.993 | 3.09 | 4.17 |
| G4 | 7.5 | 0.540 | 95.24 mg ±1.04% | 99.98 | 4.999 | 3.08 | 2.55 |
| G5 | 7.9 | 1.267 | 96.09 mg ±2.21% | 99.24 | 4.962 | 3.07 | 5.42 |

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