


EFFECT OF DILUENTS ON RELEASE PROFILE OF THEOPHYLLINE FROM TABLET DOSAGE FORM

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| <p>*For Correspondence: Padmashri Dr. Vithhalrao Vikhe Patil Foundation's College of Pharmacy, Viladghat, Ahmednagar.</p> | <p>ABSTRACT Every medicinal product is a combination of drug substance & various excipients which are indispensable components comprises the greatest proportion of dosage unit. Therefore, the knowledge of the composition, function and behavior of excipients is most important for the successful design, development and manufacturing of pharmaceutical dosage form. In the present work the effect of four different diluents namely starch, microcrystalline cellulose, mannitol and calcium sulphate dihydrate on the release of Theophylline from an immediate release tablet has been studied. The physicochemical properties such as hardness, thickness, friability, uniformity of weight and the drug content of the formulated tablets and in vitro drug dissolution study were evaluated. KEY WORDS: Diluents, Dissolution, Release profile, Theophylline.</p> |
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INTRODUCTION

The oral route of drug administration is the most important method of administering drugs for systemic effect, and the tablets are one of the most popular dosage forms because of various advantages afforded both to the manufacturer and to the patients. Diluents are used in tablet formulation to improve the bulk of the tablet and also called as fillers or vehicles. The range of diluents used in tablet may vary from 5-80%. These are mostly added into the tablets to provide better properties of tablet such as to improve or enhance bulkiness, to provide improved cohesion, to enhance the flow of the powder and to allow direct compression manufacturing.^[1,2] The present study focused on the effect of various diluents i.e., starch, microcrystalline cellulose, mannitol, and calcium sulphate dihydrate on release pattern of Theophylline from tablet dosage formulation. Theophylline is used as bronchodilator i.e. in the treatment of bronchial asthma and also Chronic Obstructive Pulmonary Disease (COPD)^[3]. Asthma is mostly encountered the bronchial disorders like recurrent inflammation of lungs which is characterized by breathing problems and various symptoms like, breathlessness, wheezing, chest tightness and coughing^[4,5]. In this work four different diluents were used and their effects on dissolution profile of Theophylline tablets were studied.

MATERIALS AND METHODS

Material:

The drug Theophylline was procured from LOBA Chemie Pvt Ltd, Mumbai. Whereas Starch, Microcrystalline Cellulose, Talc and Magnesium stearate were procured from LOBA Chemie Pvt Ltd,

Mumbai. Sodium starch glycolate was obtained from OZONE Internationals, Mumbai. Calcium sulphate dihydrate obtained from Merk Specialities, Mumbai. Mannitol was obtained from Fischer Scientific, Mumbai and Acacia were procured from SD Fine Chem Ltd, Mumbai.

Method:

Formulation and preparation of Theophylline immediate release tablets.

Theophylline tablets were prepared by wet granulation technique. In this, an accurately weighed amount of drug and other excipients except magnesium stearate and talc were mixed together in geometric fashion after passing through sieve No.100/ 80 # mesh. Then prepared solution of binder (acacia in dist. Water) was poured into the above powder mixture to form a damp mass to improve adhesion of powder particles. Then wet mass was screened into the granules. After drying the granules, lubricants were added and mixed. Then whole formula was compressed into tablets. The formula for Theophylline tablet was given in table no.1. The compressed tablets were evaluated for various properties like hardness, friability, weight variation, content uniformity, disintegration time, and dissolution time.

PRECOMPRESSION PROPERTIES [6,7,8]:

1. Angle of repose:

This was determined using fixed funnel method. In this, accurately weighed granules were taken in the funnel. The height of the funnel was adjusted to 2 cm from working platform. The powder or granules were allowed to flow freely through funnel on the surface of the platform. The height (h) and the radius of the powder cone were measured and the angle of repose were calculated using formula-Angle of repose (θ) = $\tan^{-1} h/r$

2. Bulk density:

Apparent Bulk density were calculated by taking the weighed quantity of granules in graduated cylinder and volume was measured .The bulk density was determine by using formula-Bulk Density =Mass/ bulk volume

3. Tapped Density:

The weighed sample of blend was transferred to the measuring cylinder and was tapped for fixed number of taps in the Tapped density apparatus. The tapped density were calculated by-Tapped Density =mass/tapped volume

4. Compressibility Index:

Based on the bulk density and tapped density, the compressibility index were determined as, C.I. = $\frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \times 100$

5. Hausner's Ratio:

It is an indirect index of ease of measuring of powder flow. It was measured as, Hausner's Ratio = $\frac{\text{tapped density}}{\text{bulk density}}$

EVALUATION STUDIES OF THEOPHYLLINE IMMEDIATE RELEASE TABLETS:

1. Thickness and Diameter:

These were determined by using vernier caliper in mm or cm.

2. Hardness:

The hardness of prepared tablets was determined by using Monsanto Hardness Tester in terms of Kg/cm².

3. Friability:

It was determined by using Roche friabilator. 20 tablets were selected and weighed from each batch and tested at a speed of 25 rpm for 4 minutes in which tablets were dropped from height of 6 inches in each revolution. Then tablets were dedusted and reweighed. The friability were calculated by using formula, Friability = $\frac{W_0 - W}{W_0} \times 100$

Where, W_0 = weight of tablets before test, W = weight of tablets after the test.

4. Weight variation:

In this, 20 tablets were selected randomly from the batch and weighed individually, to check weight variation, percent deviation were calculated and compared with official standards.

5. Drug Content:

20 tablets were weighed and powdered. The blend equivalent to 10 mg of Theophylline was weighed and dissolved in sufficient amount of phosphate buffer solution of Ph 6.8. The solution was filtered and diluted with same solution then assayed at 273 nm, using UV-Visible Spectrophotometer.

6. In vitro Disintegration Time:

The disintegration time were determined by using disintegration test apparatus. In this test, 6 tablets were placed individually in each tube of apparatus, disc were placed on each tablet. Distilled water used as disintegrating medium and temperature were maintained at $37 \pm 2^\circ \text{C}$. The time required for complete disintegration of the tablets with no mass remaining in the apparatus was determined.

7. In vitro Dissolution study:

It was carried out using type II paddle with 900 ml phosphate buffer solution of PH 6.8 at 50 rpm. The temperature was maintained at $37 \pm 0.5^\circ \text{C}$. The sample was withdrawn at 5 minutes interval. The sink condition was maintained by replacing with phosphate buffer solution. The samples were suitably diluted and percent drug release from each formulation was measured at 273 nm using UV-visible Spectrophotometer.

RESULT AND DISCUSSION

Precompression Properties:

Table no.2 shows information about evaluation of precompression parameters of each formulation blend of Theophylline tablets.

The table shows that all formulas have angle of repose within 14.84 - 18.21° , then Bulk density in the range of 0.33 - 0.42 , whereas, tapped density within 0.38 - 0.5 , then Carr's index in the range of 10.75 - 16.00 which concludes that all formulation blend shows better flow properties and have no major difference in their values.

Evaluation of tablets:

Table no.3 shows the observations of various parameters of tablets. The thicknesses, diameter of the all formulation batches were nearly uniform in size. Also hardness of the tablets observed within the range for all batches. The limit of friability for tablets was less than 1 % which was maintained by all the formulations batches. Figure No.1 shows comparative dissolution profile of all the batches. F1 formulation shows 98.276 % release within 35 minutes, F2 & F3 shows 97.963 % & 96.16 % release within 40 minutes respectively whereas, F3 shows 96.29% release within 45 minutes.

CONCLUSION

On the basis of literature survey, the selection of the drug candidate and the type of formulation lead to the formulation of an immediate release tablet and undergo for study of diluents on release profile of the Theophylline from tablet dosage form. The change in type of diluents i.e. starch, microcrystalline cellulose, mannitol & calcium sulphate dihydrates concludes that there is a change in dissolution profile of drug. The formulation no.1 i.e. F1 showed the better result / performance as compared to other batches. It shows that formulation F1 has percent release of 98.276 % within 35 minutes. Though all the diluents are effective for immediate release of drug but amongst all, Starch can release the drug faster as compared to other 3 diluents. The suitability order of diluents in the formulation of immediate release tablets of Theophylline was shown as below; Starch > Microcrystalline Cellulose > Calcium Sulphate Dihydrate > Mannitol.

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