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# Formulation and Evaluation of Dexlansoprazole Floating Tablets

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## Abstract

The purpose of this research was to prepare a Dexlansoprazole Gastro-Retentive Drug Delivery System. Dexlansoprazole with gas propellant with controlled release can be developed to increase the time of gastric permanence and therefore increase its bioavailability. The formulated floating tablets have given satisfactory results for various post-compressive parameters such as hardness, friability, thickness, weight variation and uniformity of the content. Sodium bicarbonate has a predominant effect on the buoyancy delay time, while chitosan has a predominant effect on the total flotation time and drug release. Carbopol also shows a significant effect in drug release. Sodium alginate and xanthan gum gave additional adhesive properties and helped maintain the integrity of the tablet. The swelling index has a significant effect on drug release.

Formulations F2 and F4 showed a higher rate of swelling than others. In vitro release rate studies showed that maximum drug release was observed in F2 and F2 formulations for up to 12 hours. TLC studies revealed that there was no interaction between dexlansoprazole and the polymers used. The data obtained from *in vitro* dissolution studies were fitted in different models viz. zero order, first order and Korsemeyer's equation. The zero order plots were found to be fairly linear as indicated by their high regression values ($r^2$ = 0.979 to 0.996). From the study it is evident that the floating tablets based on Dexlansoprazole with gas propellant with controlled release can be developed to increase the time of gastric permanence and therefore increase its bioavailability.

**Key-words:** Dexlansoprazole, floating tablets, *in vitro* buoyancy

## Introduction

It is used to treat gastroesophageal reflux disease. Efficacy is similar to that of other Proton Pump Inhibitors (PPIs). It is taken orally. Dexlansoprazole is used to treat and maintain healing of erosive esophagitis and to treat stomach acid associated with Gastroesophageal Reflux Disease (GERD). It lasts longer than lansoprazole, with which it is chemically related, and should be taken less frequently. There is no concrete evidence that it works better than other PPIs. Dexlansoprazole permanently binds to the proton pump and blocks it, preventing the formation of gastric acid. In the treatment of healing of Erosive Esophagitis (EE) 60 mg orally once a day Duration of treatment Up to 8 weeks, In the treatment of stomach acid associated with symptomatic Gastroesophageal Reflux Disease (GERD) 30 mg orally one once a day Duration of therapy 4 weeks Use [1]. The low bioavailability (40-45%) and the short biological half-life (2.5-4.0 hours) of Dexlansoprazole after oral administration favor the development of a prolonged release formulation.

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The gastroretentive drug delivery systems can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the gastrointestinal tract. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability [2].

It has been reported that the oral treatment of gastric disorders with a proton pump inhibitors (PPIs) like Dexlansoprazole used in combination with antacids promotes local delivery of these drugs to the receptor of parietal cell wall. Local delivery also increases the stomach wall receptor site bioavailability and increases efficacy of drugs to reduce acid secretion. Hence this principle may be applied for improving systemic as well as local delivery of Dexlansoprazole, which would efficiently reduced gastric acid secretion [3].

In the present investigation floating tablets of Dexlansoprazole were prepared by gas propellant with controlled release can be developed to increase the time of gastric permanence and therefore increase its bioavailability.

## Material and Methods

### Materials

Dexlansoprazole was received as a gift sample from Alembic Limited, Vadodara, India. NaHCO3, Na alginate, Chitosan, Carbopol, MCC, Xanthan gum, Lactose, Adipic Acid, Talc, Mg stearate were provided by Modern Institute of Pharmaceutical Sciences, Indore (M.P), India. All solvents used in the study are of analytical grade.

### Preformulation study [4]

The preformulation study is one of the important prerequisites for the development of any drug delivery system. It provides the information necessary to define the nature of the pharmaceutical substance and provides a structure for the combination of drugs with pharmaceutical excipients in the dosage forms.

### Drug Identification Test [5]

### Physical Appearance: (Organoleptic Character)

Dexlansoprazole was physically characterized by its appearance, color and odor. All these physical parameters were recorded and compared with the value of the literature.

Sometimes organoleptic tests are performed to determine that pharmaceutical products can transfer flavors or odors to the materials and components in which they are packaged. Life studies often use taste, sight and smell to determine if a product is safe to consume.

### Determination of melting point [6]

The determination of the melting point of the obtained sample was carried out because it is a good first indication of the purity of the sample, since the presence of a relatively small amount of impurities can be detected by a reduction and widening in the melting point range. The melting point of Dexlansoprazole was determined by the capillary fusion method; Capillary closed on one side full of drugs and placed in the melting point apparatus. The temperature at which the solid drug becomes liquid has been observed and compared with the value of the literature.

### Solubility Profile of Dexlansoprazole

Solubility can be defined as the spontaneous interaction of two or more substances to form a homogeneous molecular dispersion. A solubility analysis of the preformulation was performed, which includes the selection of the suitable solvent system to dissolve the respective drug. The solubility of Dexlansoprazole has been determined in different solvents. An excess amount of the drug in 10 ml of each solvent was added in glass tubes with screw caps and stirred for 12 hours at room temperature. The solution was filtered, diluted and then the solubility is determined.

**Table 1: Specifications of Solubility as Per I.P**

| Descriptive Terms | Approximate Volume of Solvent in milliliters per gram of solute |
|---|---|
| Very soluble | Less than 1 |
| Freely soluble | From 1 to 10 |
| Soluble | From 10 to 30 |
| Sparingly soluble | From 30 to 100 |
| Slightly soluble | From 100 to 1000 |
| Very slightly soluble | From 1000 to 10000 |
| Insoluble or practically insoluble | More than 10000 |

### Partition Coefficient Study [7]

The equal volume of n-octanol and double distilled water was saturated for a period of 24 hours. 10 mg of Dexlansoprazole were added to the mixture and stirred for 1 hour separating these two layers with the help of separating the funnel.

The aqueous phase was suitably diluted and the absorbance was taken at λmax 281 nm. The partition coefficient was calculated as the ratio between the concentration of the drug in n-octanol and that of water using the equation.

$$Po/w = (C_{Oil} / C_{water})\ equilibrium$$

**Analytical methods for the estimation of Dexlansoprazole:**

**Detection of *Absorption Maxima (max):*** The samples of the standard solution were scanned between 200-400 nm regions on Schimadzu 1800 UV spectrophotometer.

**Calibration curve for the estimation of Dexlansoprazole in methanol**

In this method, the drug Dexlansoprazole was dissolved in little amount of methanol to get the clear solution, volume was adjusted with methanol. Then the maximum absorbance was measured at 285nm. Bear's law obeyed in the concentration range 3 to 15 mcg/ml.

**Standard solution**

Dissolve 50 mg of Dexlansoprazole in few ml of methanol in 50 ml volumetric flask. The volume was adjusted to 50 ml methanol

**Stock solution**

The resultant solution subsequently diluted with methanol to get concentration of 3, 6, 9, 12 and 15 mcg/ml. the absorbance of above said concentration solution was measured at 285nm using methanol as blank.

**Flow properties of Dexlansoprazole** [8-9]

Pure Dexlansoprazole was evaluated for angle of repose, bulk density, tapped density, Hausner ratio, Carr's index, degree of homogeneity of blend.

**Angle of repose**

Angle of repose is the angle of inclination, formed to the flat surface by the bulk powder when it is allowed to flow under gravitational force from a fixed height. It is a characteristic of dry mixed powder flow properties.

$$\text{Angle of repose} = \tan^{-1} h/r$$

Where, h = Height of granules above the flat surface, r = Radius of the circle formed by the granule

**Bulk density**

Bulk density is the ratio of mass to volume of material. Bulk density of pure Dexlansoprazole and prepared mixture was determined by pouring pre-weighed powder in to a graduated cylinder. Bulk density was determined by measuring poured volume of powder and mass of powder used.

$$P_b = M / V_b$$

Where, $P_b$ =Bulk density, $V_b$ = Volume of bulk, M = Mass of powder

**Tapped density**

Tapped density was determined by placing a known mass of mixed powder into the graduated cylinder and which is operated for fixed number of taps (100) until the powder bed volume has reached a minimum. Then by measuring the volume, tapped density was determined by using the formula.

$$Pt = M / Vt$$

Where, Pt = Tapped density, Vt- Tapped volume

**Hausner ratio**

It is a simple index that can be determined on small quantity of powder and flow properties of powder may be interpreted. It was calculated by using

$$\text{Hausner ratio} = TBD / LBD \times 100$$

Where, TBD=tapped bulk density of powder, LBD= freely settled bulk density of the powder

**Carr's index**

It is a simple index that can be determined on small quantity of powder and flow properties of powder may be interpreted.

$$\text{Carr's index} = TBD - LBD / LBD \times 100$$

Where, TBD = tapped bulk density of the powder, LBD = freely settled bulk density of the powder

**Drug-excipients compatibility study** [10-11]

**Physical Observation**

It is quite common, but is very difficult to detect. A physical interaction doesn't involve any chemical changes. Physical interactions are frequently used in manufacturing of dosage form, for example to modify drug dissolution. Physical interaction can either be beneficial or detrimental to product performance. Drug alone and mixture drug and excipients were physically observed for interaction for any color, odor or powder form change.

**Thin Layer Chromatography (TLC)**

TLC is a method of chromatographic analysis performed on glass, plastic or metal plates coated on one side with a thin layer of adsorbent. The thin layer of adsorbent acts as a stationary phase

and generally consists of silica, alumina, polyamide, cellulose or ion exchange resin. In TLC, the solutions are prepared from the test samples (i.e. a mixture of the drug and of the excipients) and from the controls (single drugs and excipients) and placed on the same baseline at the end of the plate (the origin). The plate is placed in a vertical position in a closed chamber containing mixtures of organic solvents which act as a mobile phase. The analyte moves on the plate, under the influence of the mobile phase that moves through the stationary phase by capillary action. The distance traveled by the analyte depends on its relative affinity for the stationary or mobile phase. Incompatibilities are indicated by the formation of a point with an Rf value (delay factor) different from that of the controls after the plate has been developed with solvent. The drug and the excipients were mixed together in a 1:1 ratio and placed in borosilicate glass vials. These vials were sealed and placed in an oven maintained at 40 ° C and 75% relative humidity. The samples were observed after 15 and 30 days for any change in color or aggregation. The pure drug itself and the mixtures of other excipients were measured. The interaction characteristics of Dexlansoprazole, drug and polymer mixtures were analyzed by the TLC method.

Mobile phase with crude drug powder used for estimation of result

**Dexlansoprazole – Methanol: Water (2:1)**

**Method of preparation**

**Preparation of Floating tablets of Dexlansoprazole**

In the present invention, the controlled gas system (CGPS) includes a carbopol swelling agent and a gel forming polymer. Together, these agents form a hydrated gel matrix. CGPS also contains a saga generator such that a gas is generated in a controlled manner and is trapped in the component hydrated gel matrix. The gas generated by the sodium bicarbonate also causes the matrix to expand. However, in the present study, the swelling of the matrix is controlled by the viscolizador agent (xanthan gum), which acts both as a blowing agent, as a release control. The gas-generating sodium bicarbonate component interacts with a source of citric acid acidity by contact with gastric fluid to generate carbon dioxide that is trapped in the swelling composition hydrated gel matrix. In the present study, it has been found that xanthan gum helps maintain the integrity of the tablet when stirred in an aqueous medium. The sodium alginate gel polymer is cross-linked over time to form a stable structure that traps the generated gas. Thus, over time, the polymer forming gel results in a balanced hydrodynamic system in which the matrix system is maintained in the stomach for a prolonged period. Simultaneously, the viscolizador agent and gel-forming polymer provide a tortuous route spreading the drug there, resulting in controlled drug release. Hydrophilic polymers are useful in the present invention to modify the drug release rate from the tablet. It is reported that various concentrations of Chitosan lasted for buoyancy over 8 hours in simulated ground food in distilled water.

To preserve the dosage form in the stomach for a long period of time and to avoid erosion and dissolution, xanthan and Carbopol have been used as a gelling agent in combination with chitosan to delay drug release. Hydrophilic polymers such as carbopol, chitosan are used in the present study to modify the drug release rate from the tablets. Sodium bicarbonate ($NaHCO_3$) has been incorporated into the formulation so that when it comes into contact with the acidic gastric contents, the $CO_2$ is released and trapped in inflamed hydrocolloids, which provides buoyancy to the dosage form. Lactose has been included in the formulation as a hydrophilic agent, assuming that the capillary action of lactose can facilitate greater drug release without affecting the matrix (buoyancy capacity), the incorporation of lactose has shown an adequate release and a time of floatation. In all the formulations designed, the weight of a single tablet remained constant. The weight of a single tablet was 260 mg.

**Formulation Development**

**Table 2: Method of Preparation**

| INGREDIENTS | F1 (mg) | F2 (mg) | F3 (mg) | F4 (mg) |
|---|---|---|---|---|
| Dexlansoprazole | 60 | 60 | 60 | 60 |
| $NaHCO_3$ | 20 | 40 | 50 | 50 |
| Na alginate | 10 | 20 | 20 | 20 |
| Chitosan | 10 | 10 | 20 | 20 |
| Carbopol | 30 | 20 | 20 | 20 |
| MCC | 30 | 20 | 20 | -- |
| Xanthan gum | 10 | -- | 10 | 10 |

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| | | | | |
|---|---|---|---|---|
| Lactose | 40 | 30 | 20 | 20 |
| Adipic Acid | 10 | 10 | 10 | 10 |
| Talc | 10 | 20 | - | 20 |
| Mg stearate | 30 | 30 | 30 | 30 |

**Evaluation of Post-Compressional Parameters of Tablets** [12]

**Weight variation:**

Twenty tablets were randomly selected and individually weighed. The average weight of 20 tablets was calculated. The individual tablet weights were compared to the average weight.

**Table 3: IP Standards for uniformity of weight**

| Sr. No | Average weight of tablet | Percentage of deviation |
|---|---|---|
| 1 | <80mg | 10 |
| 2 | 80 – 250 mg | 7.5 |
| 3 | >250mg | 5 |

**Hardness:**

The hardness of the tablet was defined as the force required to break a tablet in a diametral compression test.

**Friability:**

The tablets require a certain amount of strength or hardness and strength to withstand the mechanical shock of handling in production, packaging and shipping. A pre-weighed sample (20 tablets) was placed in the crusher and run for 100 revolutions, then the tablets were weighed again and the friability percentage was calculated using the formula.

$$F = 1 - W_o / W \times 100$$

Where, $W_o$=Weight of tablet before test, $W$= Weight of tablet after test

**Tablet thickness, diameter and hardness**

All the formulations were evaluated for various parameters, like thickness, diameter and hardness of all tablets from batch F1 to F4.

**Drugs content:**

To assess the effectiveness potential of a tablet, the amount of drug per tablet must be controlled from one tablet to another and from one batch to another. To perform the test, 10 tablets were crushed with mortar. An amount equivalent to 100 mg of drug was dissolved in 100 ml. Methanol is filtered and diluted to 50 µg / ml and analyzed spectrophotometrically at 285 nm. The drug concentration was determined using a standard calibration curve.

**Buoyancy determination:**

The buoyancy test of the tablet was studied by placing it in a 200 ml beaker containing 0.1 N of HCl, then the tablet of the same lots was placed in a dissolution test apparatus containing 900 ml of HCl 0, 1N, is was maintained at 37 ± 0.5 ° C and was stirred at 50 rpm. The floating starts time (the period of time between the positioning of the tablet in the center and the start of the buoyancy) and the duration of the tablet was determined by visual observation.

***In-vitro* dissolution study** [13]

The in vitro dissolution test was performed using the USP type II dissolution test apparatus. The drug release study was conducted in 0.1 N HC1 for 12 hours in 900 ml dissolution medium, maintained at 37 ± 0.5 ° C and stirred at 100 rpm. Periodically, 5 ml of samples were removed and filtered through the Whatman filter paper and the samples were replaced by their equivalent volume of dissolution medium. The concentration of Dexlansoprazole was measured spectrophotometrically at 285 nm.

**Swelling characteristics (Water uptake study)** [14]

The swelling properties of HPMC matrices containing drug were determined by placing the tablet matrices in the dissolution test apparatus, in 900 ml of distilled water at 37 ± 0.5°C paddle rotated at 50 rpm. The tablets were removed periodically from dissolution medium. After draining free from water by blotting paper, these were measured for weight gain. Swelling characteristics were expressed in terms of percentage water uptake (WU %) according to the equation.

**% WU = Weight of swollen tablet – initial wt of tablet/ initial wt of tablet × 100**

## Results and Discussion

**Preformulation Studies**

**Drug Identification Test**

**Organoleptic Properties**

The sample of Dexlansoprazole was identified for colour, odour which was found to be same as that of standard parameters.

**Table 4: Organoleptic Properties of Dexlansoprazole**

| S. no | Parameters | Sample |
|---|---|---|
| 1 | Colour | White |
| 2 | Odour | Odorless |

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**Melting Point**

The melting point of Dexlansoprazole was found to be 140 °C and the drug was found to be in the pure form.

**Table 5: Melting point of Dexlansoprazole**

| S. no | Range | Melting point |
|---|---|---|
| 1. | 138-142°C | 140°C |

**Solubility Studies**

The solubility of the drug sample was determined by accurately weight 10 mg of Dexlansoprazole was added in 6 test tubes and was added in aqueous and non aqueous solvents and solution was kept for 24 hrs and then samples were analyzed by U.V visible spectrophotometry and were found to be soluble in polar and were found to be insoluble in non polar solvents.

**Table 6: Solubility Profile of Dexlansoprazole in Aqueous and Non Aqueous Solvents**

| S. No. | Solvent | Solubility |
|---|---|---|
| 1 | 0.1N HCl | Soluble |
| 2 | Water | Soluble |
| 3 | Methanol | Soluble |
| 4 | Ethanol | Soluble |
| 5 | Chloroform | Insoluble |

**Partition Coefficient Study:**

Equal volume of n-octanol and double distilled water were saturated for a period of 24 h. 10 mg of Dexlansoprazole was added to the mixture and was agitated for 1 hr. separating these two layers with the help of separating funnel. Water phase was then diluted suitably and absorbance was taken at $\lambda_{max}$ 281 nm. Partition coefficient was calculated as the ratio of drug concentration in n-octanol to that in the water using equation

$$P_{o/w} = (C_{Oil} / C_{water}) \text{ equilibrium}$$

The partition value was calculated and compared with literature value.

**Partition Coefficient Values of Dexlansoprazole in n-Octanol: Distilled Water**

**Table 7: Solubility Profile of Dexlansoprazole in Aqueous and Non Aqueous Solvents**

| Medium | Experimental value | Literature value |
|---|---|---|
| Distilled water | 1.9 ± 0.76 | 2.38 |

**Determination of suitable wavelength**

The UV spectrum of Dexlansoprazole from 200-400 nm and is illustrated in figure. The spectrum indicates that 285 nm gives a good sensitivity for of Dexlansoprazole.

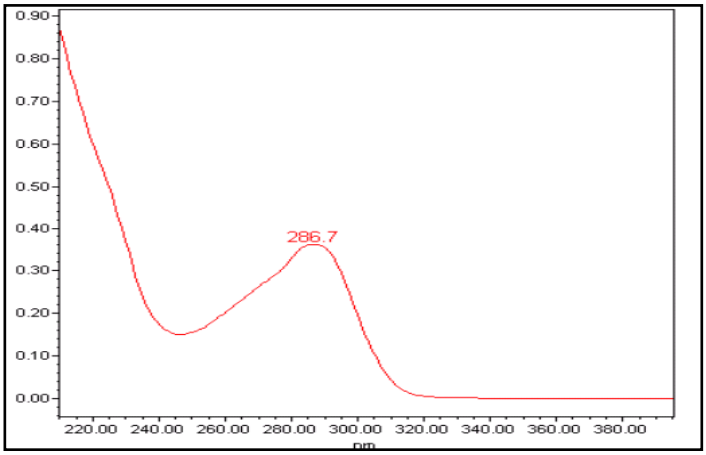


**Figure 1: UV spectra of Dexlansoprazole**

**Calibration curve of Dexlansoprazole:**

Then the maximum absorbance was measured at 285nm. Bear's law obeyed in the concentration range 3 to 15 mcg/ml

**Table 8: Absorbance values for standard Dexlansoprazole in methanol**

| Concentration (mcg/ml) | Absorbance |
|---|---|
| 0 | 0 |
| 3 | 0.127 |
| 6 | 0.265 |
| 9 | 0.368 |
| 12 | 0.512 |
| 15 | 0.628 |

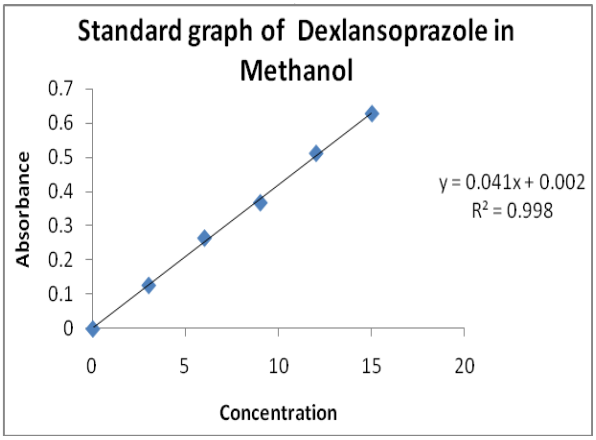


**Figure 2: Standard calibration data of Dexlansoprazole in methanol**

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**Flow properties of Dexlansoprazole**

Powder flow is very important in a production process. The mixing process with a low fluidity powder is terrible and it would not be possible to guarantee the uniformity of the content for each pill or tablet. The compression process, the formation of tablets, would entail a great weight variation.

**Table 9: Flow properties of Dexlansoprazole**

| S. No. | Flow property | Observation |
|---|---|---|
| 1. | Angle of repose | 34.37° |
| 2. | Bulk density | 0.378 g/$m^3$ |
| 3. | Tapped density | 0.389g/$m^3$ |
| 4. | Hausner's ratio | 1.23 |
| 5. | Carr's index | 13.25 % |

**Drug-Excipients Compatibility Study**

**Physical Observation**

The physical compatibility was observed visually. The study reveals that the drug and the excipients were physically compatible with each other as there was no change of color. The excipients are compatible with the drug selected for the formulation.

**Table 10: Physical Compatibility of Paracetamol and Excipients**

| Drug + Excipients | Description and Condition | Room Temperature and 40°C/75% RH in days | | |
|---|---|---|---|---|
| | | Initial | 15th | 30th |
| **Dexlansoprazole** | White powder | NC | NC | NC |
| **$NaHCO_3$** | White crystalline powder | NC | NC | NC |
| **Na alginate** | Colorless crystalline | NC | NC | NC |
| **Chitosan** | Yellow to white | NC | NC | NC |
| **Carbopol** | White powder | NC | NC | NC |
| **MCC** | White fine powder | NC | NC | NC |
| **Xanthan gum** | White powder to faintly yellow | NC | NC | NC |
| **Lactose** | White crystalline powder | NC | NC | NC |
| **Adipic Acid** | White crystalline powder | NC | NC | NC |
| **Talc** | White fine powder | NC | NC | NC |
| **Mg stearate** | White fine powder | NC | NC | NC |

**NC* - No Change**

**Thin Layer Chromatography (TLC)**

The study reveals that the drug and the excipients were chemically compatible with each other as there was no significant change in the Rf values.

**Table 11: Chemical Compatibility of Dexlansoprazole and Excipients**

| Dexlansoprazole +Excipients | Room Temperature 40°C & 75% RH in days | | | | | | Result |
|---|---|---|---|---|---|---|---|
| | Initial | | 15th | | 30th | | |
| | $Rf_1$ | $Rf_2$ | $Rf_1$ | $Rf_2$ | $Rf_1$ | $Rf_2$ | |
| **Dexlansoprazole** | 0.59 | 0.51 | 0.51 | 0.46 | 0.51 | 0.58 | NC |
| ***D + $NaHCO_3$** | 0.56 | 0.55 | 0.52 | 0.40 | 0.55 | 0.63 | NC |
| **D + Na alginate** | 0.44 | 0.61 | 0.50 | 0.36 | 0.53 | 075 | NC |
| **D + Chitosan** | 0.42 | 0.46 | 0.63 | 0.61 | 0.61 | 0.50 | NC |
| **D + Carbopol** | 0.72 | 0.76 | 0.52 | 0.45 | 0.61 | 0.50 | NC |
| **D + MCC** | 0.62 | 0.61 | 0.50 | 0.56 | 0.55 | 0.68 | NC |
| **D + Xanthan gum** | 0.31 | 0.36 | 0.55 | 0.59 | 0.36 | 0.40 | NC |
| **D + Lactose** | 0.56 | 0.53 | 0.53 | 0.52 | 0.61 | 0.63 | NC |
| **D + Adipic Acid** | 0.72 | 075 | 0.48 | 0.53 | 075 | 0.62 | NC |
| **D + Talc** | 0.46 | 0.42 | 0.45 | 0.41 | 0.38 | 0.59 | NC |
| **D + Mg stearate** | 0.82 | 0.79 | 0.66 | 0.52 | 0.60 | 0.53 | NC |

$Rf_1^*$ = standard value & $Rf_2^*$ = sample value. D*= Dexlansoprazole

NC* - No Change

**Evaluations of dry mixed powder blend for Precompressional parameters**

The granulation characteristics are the most important interest to formulation scientist and therefore most universally measured. These basic measurements of the granulation have been used to develop and monitor the manufacture of many successful pharmaceutical dosage forms.

Bulk density may influence compressibility, tablet porosity, dissolution and other properties and depends on the particle size, shape and tendency of particles to adhere together. The bulk density of powder blend was found to be between 0.3061 ± 0.04 to 0.3694 ± 0.04 g/$cm^3$. This indicates good packing capacity of powder blend. Carr's index was evaluated. Interparticulate cohesive properties with angle of repose measurements and the effects of packing geometry of solids with bulk and tapped density were studied. Bulk density and tapped density measurements found that density of a powder depends on particle packing and that density changes as the powder consolidates. The degree of consolidation is unique to the powder

and ratio of these densities is related to interparticulate friction. This ratio, percent compressibility, was used as an index of flow. Adhesive/cohesive forces of particles are related to flow behavior. Values of Carr's index below 15% usually show good flow characteristics, but readings above 25 % indicate poor flow ability. Carr's index was found to be between 14.89 ± 0.03 to 21.06 ± 0.11. Hausner's ratio is simple method to evaluate stability of powder column and to estimate flow properties. Low range was observed in Hausner's ratio that indicates good flowing ability. Many different types of angular properties have been employed to assess flowing ability. Angle of repose is suited for particles >150µm

Angle of repose of 30° generally indicates the free flowing material and angle of 40° suggest a poor flowing material. The angle of repose is indicative of the flowing ability of the material. The angle of repose of all the formulations fell within the range of 19.09 ±0.017 to 29.24 ± 0.09 i.e. granules were of good flow properties. Results are shown in the table.

**Table 12: Precompressional data**

| Batch No. | Bulk Density (gm/cm3) | Tapped Density (gm/cm3) | Carr's Index (IC ) | Hausner Ratio (HR) | Angle of Repose |
|---|---|---|---|---|---|
| F1 | 0.3432±0.04 | 0.4165±.05 | 21.35±0.07 | 1.21±0.03 | 24.92±0.08 |
| F2 | 0.3648±0.06 | 0.4262±0.03 | 16.83±0.01 | 1.16±0.08 | 29.48±0.10 |
| F3 | 0.3322±0.04 | 0.3950±0.04 | 16.94±0.07 | 1.18±0.05 | 25.24±0.17 |
| F4 | 0.3655±0.05 | 0.4156±0.06 | 13.70±0.07 | 1.13±0.07 | 26.07±0.18 |

**Evaluation of post Compressional parameters of tablet characteristics**

The floating tablets of Dexlansoprazole were prepared with direct compression technique. The tablets were evaluated for average weight, thickness, hardness, friability and drug content.

**Tablet thickness, Diameter and Hardness**

Since there was not much variation in the thickness of the tablets in each formulation, it shows that the powder mixtures were consistent in particle size and uniform behavior during the compression process. The thickness and diameter of the tablets of all the batches were measured with a vernier calibrator and there will be no changes in the thickness and diameter of the tablets, respectively. The thickness was between 4.20 ± 0.04 and 4.50 ± 0.04. The hardness of the tablet was measured on a Monsanto hardness meter in a range between 7 and 9 kg / cm2. The hardness of the tablet reflects the differences in density and porosity of the tablet, which should produce different drug release patterns influencing the rate of dissolution liquid penetration on the tablet surface.

**Friability of Tablet**

The present study of tablets is within the limit and the slight variation in friability is because of the variation in compression force applied and its total weight. The friability of tablets also depends on type of filler and moisture content.

**Table 13: Evaluation of post Compressional Parameters of Tablet Characteristics**

| Batch no. | Average wt. (mg) | Thickness (mm) | Diameter (mm) | Hardness (kg/cm$^2$) | Friability (%) |
|---|---|---|---|---|---|
| F1 | 596 | 4.20±0.03 | 12.10±0.05 | 7.50±0.01 | 0.78±0.041 |
| F2 | 600 | 4.35±0.04 | 12.08±0.02 | 8.40±.02 | 0.77±0.039 |
| F3 | 597 | 4.20±0.02 | 12.05±0.03 | 9.0±0.04 | 0.75±0.044 |
| F4 | 602 | 4.40±0.04 | 12.06±0.02 | 7.0±0.03 | 0.66±0.039 |

**Drug Content and Swelling Index Study**

**Drug Content:**

Drug content was in range of 96.38±0.12 to 106.44±0.12 indicating good content uniformity in all formulations. That indicates drug was uniformly distributed throughout the tablet.

**Swelling Index:**

Results of water uptake study showed that the order of swelling in these polymers could indicate the rates at which the preparations are able to absorb water and swell. Maximum liquid uptake and swelling of polymer was achieved up to 12 hrs and then gradually decreased due to erosion.

The swelling of polymers used in this CGPS tablets (Chitosan, carbopol, sodium alginate) could be determined by water uptake of the tablets. The complete swelling was achieved by the end of 12 hrs. The % of swelling of F4 was higher due to increase in the concentration of carbopol which also gives the firm structure to the tablet form.

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**Table 14: Drug Content and Swelling Index Study**

| Batch No. | Drug content (%) | Swelling index |
|---|---|---|
| F1 | 101.18±0.13 | 68.42±0.80 |
| F2 | 108.63±0.12 | 96.56±0.56 |
| F3 | 102.71±0.22 | 34.26±0.23 |
| F4 | 104.91±0.15 | 51.68±0.14 |

**In-Vitro Buoyancy and Lag Time Study**

From the results obtained, it was found that formulation F2 did not float. This was due to the lower percentage of gas generating agent and high concentrations of carbopol polymer. The formulation F1, F3 floated but the lag time was more and floating time is less. For the formulations F1 the duration of buoyancy was more than 12 hrs, the floating capacity increased in these formulation and floated with less lag time due to high concentration of gas generating agent. It was observed that paddle speed affected the floating properties of tablet. In the study with 200 ml 0.1N HCL without paddle it was found that the floating lag time decreased and the duration increased for the same formulations.

It was seen that as carbopol 934P concentration decreased, the floating capacity increased. However, some results revealed that, as the concentration of chitosan increased, total floating time increased, this is because of increased gel strength of matrices, which prevents escape of evolved carbon dioxide from matrices, leading to decreased density of the formulations. In the present invention, it has found that a xanthan gum helps in maintaining tablet integrity. As the amount of polymer in the tablet formulation increases, the drug release rate decreases and as the concentration of gas generating agent ($NaHCO_3$) increases the drug release increases and at the same time floating lags time decreases.

***In-vitro* release study of CGPS floating tablets of Dexlansoprazole:**

In-vitro release data of all the formulations were given in table at the end of 6 hrs and 12 hrs. The releases of Dexlansoprazole from all the formulations were in the range of 38.48 ± 5.34 to 68.18 ± 1.34 at the end of 6 hr and 54.52 ± 0.69 to 97.35 ± 1.09 at the end of 12 hrs. The formulations F1, F2, F3 and F4 released the drugs in the range 62.43- 96.85% at the end of 12 hrs respectively.

**After 1 min After 1 Hr After 12 Hr**
**Figure 3: *In-vitro* Buoyancy Study**

**Table 15: Floating ability of various CGPS Dexlansoprazole tablet formulation**

| Batch No. | Floating Lag time (min) | Floating duration (min) Integrity |
|---|---|---|
| F1 | 48 | 60 |
| F2 | 60 | 60 |
| F3 | 34 | 480 |
| F4 | 12 | 180 |

The detailed in vitro data were plotted for percentage drug released Vs time.

From the dissolution study it was concluded that release from the matrix is largely dependent on the polymer swelling, drug diffusion and matrix erosion. The drug release study is carried out up to 12 hrs. The percentage drug release from batch F1 to F4 vary from 62.43- 96.85%. All the formulations were designed as dosage forms for 12 hrs. The results suggest that therapeutic levels of Dexlansoprazole can be delivered in the controlled manner. It may be concluded that, the CGPS Dexlansoprazole tablet formulations F2 and F4 show promising controlled drug release. And formulation F4 shows the best results.

**Table 16: *In-vitro* % drug release data at the end of 12 hrs from CGPS**

| Batch No. | 1 hr | 2hrs | 4hrs | 6hrs | 8hrs | 10hrs | 12hrs |
|---|---|---|---|---|---|---|---|
| F1 | 7.8±0.6 | 13.5±0.91 | 21.88 ±1.6 | 35.5±0.8 | 42.64 ±0.9 | 50.93 ±1.2 | 62.43 ±0.23 |
| F2 | 8.62±0.69 | 19.25 ±0.4 | 29.42 ±2 | 40.68 ±0.9 | 60.01 ±1.2 | 75.28 ±0.9 | 80.93 ±0.2 |
| F3 | 6.48±0.3 | 12,26 ±0.4 | 25.68 ±0.5 | 37.48 ±3 | 47.67 ±2 | 52.68 ±4 | 68.45 ±0.4 |
| F4 | 9.96±0.5 | 25.64 ±0.6 | 32.32 ±0.7 | 49.86 ±0.3 | 66.23 ±0.7 | 79.38 ±0.6 | 96.85 ±0.8 |

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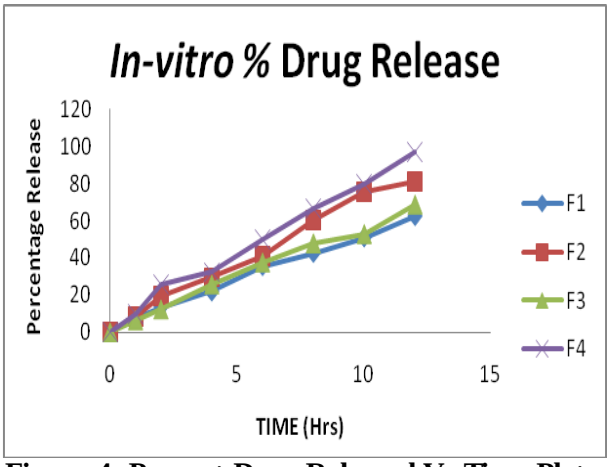


**Figure 4: Percent Drug Released Vs Time Plots of formulations F1 to F4**

**Release kinetics:**

The data obtained from *in vitro* dissolution studies were fitted in different models viz. zero order, first order and Korsemeyer's equation. The zero order plots were found to be fairly linear as indicated by their high regression values ($r^2$ = 0.979 to 0.996). To confirm the exact mechanism of drug release from these tablets, the data were fitted according to Korsemeyer's equation [8-9]. Regression analysis was performed and regression values '$r^2$' were 0.982 to 0.998 for different formulations. Slope values (0.5<n<1.0) suggest that the release of Dexlansoprazole from floating tablets followed non-Fickian transport mechanism.

**Table 17: Kinetics of *In Vitro* Dexlansoprazole Release from Floating Tablets**

| Code | Zero Order | | First Order | | Korsemeyer Model | |
|---|---|---|---|---|---|---|
| | k0 (mg. $h^{-1}$) | $r^2$ | k1 ($h^{-1}$) | $r^2$ | n | $r^2$ |
| F1 | 9.984 | 0.988 | -0.237 | 0.959 | 0.737 | 0.982 |
| F2 | 7.494 | 0.979 | -0.186 | 0.938 | 0.680 | 0.998 |
| F3 | 8.459 | 0.990 | -0.117 | 0.975 | 0.897 | 0.992 |
| F4 | 9.458 | 0.995 | -0.122 | 0.959 | 0.853 | 0.989 |

## Conclusion

From the study it is evident that the floating tablets based on Dexlansoprazole with gas propellant with controlled release can be developed to increase the time of gastric permanence and therefore increase its bioavailability. More detailed investigations are needed to establish the effectiveness of these formulations and to set the required dose.

The formulated floating tablets have given satisfactory results for various post-compressive parameters such as hardness, friability, thickness, weight variation and uniformity of the content. Sodium bicarbonate has a predominant effect on the buoyancy delay time, while chitosan has a predominant effect on the total flotation time and drug release. Carbopol also shows a significant effect in drug release. Sodium alginate and xanthan gum gave additional adhesive properties and helped maintain the integrity of the tablet. The swelling index has a significant effect on drug release. Formulations F2 and F4 showed a higher rate of swelling than others. In vitro release rate studies showed that maximum drug release was observed in F2 and F2 formulations for up to 12 hours. TLC studies revealed that there was no interaction between dexlansoprazole and the polymers used. The data obtained from *in vitro* dissolution studies were fitted in different models viz. zero order, first order and Korsemeyer's equation. The zero order plots were found to be fairly linear as indicated by their high regression values ($r^2$ = 0.979 to 0.996).

From the study it is evident that the floating tablets based on Dexlansoprazole with gas propellant with controlled release can be developed to increase the time of gastric permanence and therefore increase its bioavailability. More detailed investigations are needed to establish the effectiveness of these formulations and to set the required dose.

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