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# FORMULATION AND EVALUATION OF IMMEDIATE RELEASE TABLET OF TRAZODONE HCl BY USING IMMEDIATE RELEASE DIRECT COMPRESSION TECHNIQUE

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***Abstract:***
The Present study was carried out with Trazodone Hydrochloride by Direct Compression technique with help of different ratio of excipients and xylitol. The disintegrate the tablet as quick as possible to improve the dissolution of the drug. To develop a physically and chemically stable and Immediate release tablets. The employing suitable technique i.e., Direct Compression and evaluate the formulation of Trazodone HCl Immediate Release Tablets better formulation to disintegrate the tablet as quick as possible to improve the dissolution of the drug. The Immediate Release Tablets characterized by FTIR, UV, solubility study and dissolution studies in different kinetics models.
***Keyword:*** Direct Compression Technique, UV, FTIR, Dissolution Studies, Kinetic Models

## INTRODUCTION

These dosage forms rapidly disintegrate and/or dissolve to release the drug as soon as they come in contact with saliva, thus obviating the need for water during administration, an attribute that makes them highly attractive for pediatric and geriatric patients. Difficulty in swallowing conventional tablets and capsules is common among all age groups, especially in elderly and dysphagic patient , Common complaints about the difficulty in swallowing tablets in the order of frequency of complaints are size, surface, form, and taste of tablets. Geriatric and pediatric patients and traveling patients who may not have ready access to water are most in need of easy swallowing dosage forms. Another study shows that an estimated 50% of the population suffers from this problem. These studies show an urgent need for a new dosage form that can improve patient compliance. Solid dosage forms that can be dissolved or suspended with water in the mouth for easy swallowing are highly Immediate Release for the pediatric and geriatric population, as well as other patients who prefer the convenience of readily administered dosage forms. The European Pharmacopoeia defines the term “orodisperse” as a tablet that can be placed in the mouth where it disperses rapidly before swallowing. Suitable drug candidates for such systems include neuroleptics, cardiovascular agents, analgesics, antiallergics and drugs for erectile dysfunction. Mouth dissolving of tablet results in quick dissolution and rapid absorption which provide rapid onset of action. Moreover, drug candidates that undergo pre-gastric absorption when formulated as Immediate Releases may show increased oral bioavailability. It provides good stability, accurate dosing, and easy manufacturing.

## MATERIALS AND METHODS

### 1. MATERIALS

The few materials such as drug and excipients it was obtained as gift sample from following industry. The Remaining was obtained as analytical grade from laboratory. The few materials such as drug and excipients it was obtained as gift sample from following industry. Remaining was obtained as analytical grade from laboratory.

Table No. 1: List of Material used

| Sr. No. | Material Used | Procured from |
|---|---|---|
| **Drug** | | |
| 1 | Trazodone HCl HCl | Intelliscend NDDR Thane |
| **Excipients** | | |
| 2 | Colloidal Silicon Dioxide | Evonik India Pvt. Ltd |
| 3 | Lactose Anhydrous 21AN | Lobachemie |

| | | |
|---|---|---|
| 4 | Xylitol | Research lab |
| 5 | Sodium starch glycolate | Holden Pharmaceutical Laboratories Pvt Ltd |
| 6 | Magnesium stearate | Lobachemie |
| 7 | Microcrystalline Cellulose 302 | FMC |

## 2. METHODS

### 2.1 PREFORMULATION STUDY

Preformulation testing is the f Immediate Release step in rational development of any dosage forms of a drug substance. Preformulation study is the process of optimizing the delivery of drug through determination of physicochemical properties of the new compound that could affect drug performance and development of an efficacious, stable and safe dosage form. It gives the information needed to define the nature of the drug substance and provide a framework for the drug combination with pharmaceutical excipients in the dosage form. Hence, preformulation studies were performed for the obtained sample of drug for identification and compatibility studies.

### 2.2 CHARACTERIZATION OF DRUG CANDIDATE

#### 2.2.1 Identification of Trazodone Hydrochloride

The sample of Trazodone HCl obtained was subjected to identification by its melting point, solubility, Immediate Release, UV, and Differential Scanning Calorimetry thermogram determination.

#### 2.2.2 Melting Point

The melting point of drug was determined by Melting point apparatus using capillary method. The observed value was compared with the reported value.

#### 2.2.3 Solubility

Solubility of the drug is one of the considerations in oro-dispersible tablet formulations.Solubility was determined by dissolving pure drug in various solvents like water, alcohol, acetone & dichloromethane

#### 2.2.4 Infrared absorption Spectrophotometry

The drug is determined by infrared absorption spectrophotometer by using FTIR. The spectrum was compare with that obtained with paracetamol RS or with the reference spectrum of Trazodone HCl.

#### 2.2.5 UV Identification/Determination

Serial concentrations of Trazodone HCl hydrochloride in 0.1 N hydrochloride buffer (pH 1.2) having concentrations between 10 and 70 mcg/ml were prepared. The absorbance of the prepared solutions was measured spectrophotometrically at λmax 278 nm. The absorbance was plotted against the concentration and regression lines

#### 2.2.6 Loss on drying:

It was determined on 1.0 g by drying in an oven at 105º. It was found not more than 0.5 %.

#### 2.2.7 Preparation of Standard Stock Solution

The standard stock solution was prepared by dissolving Trazodone HCl in 0.1 N hydrochloride buffer (pH 1.2) to make final concentration of 70µg/ml (70 ppm). Different aliquots were taken from stock solution and diluted with pH 1.2separately to prepare series of concentrations from 10-70µg/ml. The λmax was found to be 278 nm from UV spectrum of Trazodone HCl inpH 1.2, during scanning from 200-400 nm. Absorbance was measured at 278 nm against pH 1.2as blank on UV-Visible Spectrophotometer (shimadzu1800). The observations were recorded and the calibration curve was prepared by plotting absorbance versus concentration of Trazodone HCl. All the excipients were characterized for its odour, appearance, nature, Immediate Release, solubility and for microscopic determination.

Appearance and Nature, Appearance and nature of the excipient were observed by visual observation.

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### DRUG-EXCIPIENTS COMPATIBILITY STUDY

A compatibility study was carried out with potential formulation excipients to determine drug-excipients interaction. All the physical mixtures of drug and excipients in 1:1 ratio and for drug and lubricant or glidant in 20:1 was kept under compatibility study for 14 days at 55°C in glass vials sealed. The physical mixtures were taken in same ratio as that of actual formulation ratio and were observed physically. The Caking, Liquefaction, Discoloration, and Odour or gas formation.Physical observations for any change in appearance were recorded.

Table No.2: Feasibility Trial Batches for Tablet (Trial 1 for 100 Tablets 400mg)

| Ingredients | Qt. Given (mg) | Qt. Taken (gm) 100 Units |
|---|---|---|
| Trazodone HCl | 100.00 | 10.0 |
| Lactose Anhydrous | 95.00 | 9.5 |
| Colloidal Silicon Dioxide | 10.00 | 1.0 |
| SSG | 25.00 | 2.5 |
| MCC 302 | 160.00 | 16.00 |
| Xylitol | 5.00 | 0.5 |
| Magnesium Stearate | 5.00 | 0.5 |
| **Total weight (mg)** | **400.00** | **40.00** |

**Justification:** The DT has been increases due to more concentration of Lactose.

Table No. 3: Feasibility Trial Batches for Tablet (Trial 2 for 100 Tablets 400mg)

| Ingredients | Qt. Given(mg) | Qt. Taken (gm) 100 Units |
|---|---|---|
| Trazodone HCl | 100.00 | 10.0 |
| Lactose Anhydrous | 20.00 | 2.0 |
| Colloidal Silicon Dioxide | 10.00 | 1.0 |
| SSG | 25.00 | 2.5 |
| MCC 302 | 235.00 | 23.5 |
| Xylitol | 5.00 | 0.5 |
| Magnesium Stearate | 5.00 | 0.5 |
| **Total Weight (mg)** | **400.00** | **40.0** |

**Justification:** The DT has been decreases due to less concentration of Lactose.

Table No. 4: Feasibility Trial Batches for Tablet (Trial 2 for 100 Tablets 360mg)

| Ingredients | Qt. Given (mg) | Qt. Taken (gm) 100 Units |
|---|---|---|
| Trazodone HCl | 100.00 | 10.0 |
| Lactose Anhydrous | 50.00 | 5.0 |
| Colloidal Silicon Dioxide | 10.00 | 1.0 |
| SSG | 25.00 | 2.5 |
| MCC 302 | 165.00 | 16.5 |
| Xylitol | 5.00 | 0.5 |
| Magnesium Stearate | 5.00 | 0.5 |
| **Total Weight (mg)** | **360.00** | **36.0** |

**Justification**: Lastly the batch DT and Hardness shows appropriately.

## 3. FACTORIAL DESIGN

Instead of repeating experiment for each independent variable or factor, we can design a more efficient experiment that evaluates the effect of two or more factors at some time. These types of design are referred to as factorial design.

In full factorial design responses are measured at all combination of the experiment factors levels. The combination of factor levels represents the condition at which response will be measured. Each experiment condition is run. The response measurement is an observation. The Immediate Release set of runs is the design. Full factorial design is generally use to determine which variable are the most influential on response or to determine the interaction between/ among two or more factors that influence the response.

### 3.1 Following terms are used in factorial design

**3.1.1 Factors:** It is a variable which affects the result of experiment. The determination of factor for particular experiment depends mainly on the objective of the experiment and it needs to be determining after careful evaluation of results.

**3.1.2 Level:** It is the limit of variable below or beyond which an experiment cannot give significant change in results.

Table No.5: Factorial design

| Formulation Code | Variable level code | |
|---|---|---|
| | $X_1$ | $X_2$ |
| F1 | -1 | -1 |
| F2 | -1 | 0 |
| F3 | -1 | +1 |
| F4 | 0 | -1 |
| F5 | 0 | 0 |
| F6 | 0 | +1 |
| F7 | +1 | -1 |
| F8 | +1 | 0 |
| F9 | +1 | +1 |

Table No.6: Formulation trial with $3^2$ full factorial design

| Factors | Levels | | |
|---|---|---|---|
| | Low | Medium | High |
| $X_1$ | -1 | 0 | +1 |
| $X_2$ | -1 | 0 | +1 |

Where,X1= SSG

X2= MCC 302

Table No.7: Value codes of factorial design value codes of factorial design in (%)

| Factors | Levels (%) | | |
|---|---|---|---|
| | Low | Medium | High |
| Sodium Starch Glycolate | 5.55% | 6.94% | 8.33% |
| MCC 302 | 44.44% | 45.83% | 47.22% |

**3.2 Formulation of trial batches by using different concentration of SSG and Mannitol:**

The formulation trial was taken with combination of SSG and MCC 302. In 9 batches (F1-F9) concentration of Lactose and Xylitol were kept constant to obtained optimized formulation. The tablets were made by Direct compression method. The tablet compression was carried out on Jaguar eight station tablet press using 10 mm punch.

Table No.8: Formulation of factorial design batches from F1-F9

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Trazodone HCl | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Lactose Anhydrous | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| SSG | 20 | 20 | 20 | 25 | 25 | 25 | 30 | 30 | 30 |
| MCC 302 | 160 | 165 | 170 | 160 | 165 | 170 | 160 | 165 | 170 |
| Aerosil 200 Pharma | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Xylitol | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Magnesium Stearate | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **Total Weight** | **360** | **360** | **360** | **360** | **360** | **360** | **360** | **360** | **360** |

The characterization of diluents was done by measuring % spray dried yield, Moisture content, Bulk Density, Tapped Density, Compressibility Index, Angle of Repose and Hausner's Ratio which was compare with dried diluents to observe the difference.

**3.3 Moisture content**

Moisture content was determined at 0% relative humidity created with calcium carbonate in desiccator. The sample (initial weight) was kept in desiccator and observed the weight loss (final weight), %moisture content was calculated using following formula,

$$\text{Percent moisture content} = \frac{\text{Initial weight - final weight}}{\text{Final weight}} \times 100$$

**3.4 Bulk Density**

Apparent bulk density ($\rho$ b) was determined by pouring the blend into a graduated cylinder. The bulk volume (Vb) and weight of the powder (M) was determined. The bulk density ($\rho$ b) was calculated using following formula,

$$\rho_b = \frac{V_b}{M}$$

**3.5 Tapped Density**

The measuring cylinder containing a known mass of blend (M) was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and weight of the blend was measured. The tapped density ($\rho$ t) was calculated using following formula,

$$\rho_t = \frac{V_t}{M}$$

**3.6 Compressibility Index**

The simplest method of measurement of free flow of powder is compressibility, an indication of the ease with which material can be induced to flow is given by compressibility index (I) which is calculated as follows,

$$I = \frac{\rho_t - \rho_b}{\rho_t} \times 100$$

Table No. 9: Carr's index as an indication of powder flow

| Sr No. | Carr's index (%) | Type of flow |
|---|---|---|
| 1 | 5-12 | Excellent |
| 2 | 12-16 | Good |
| 3 | 18-21 | FaImmediate Release |
| 4 | 23-35 | Poor |
| 5 | 33-38 | Very poor |

**3.7 Hausner's Ratio (H)**

This is an index of ease of powder flow. It is calculated by the following formula,

$$\mathrm{H} = \frac{\rho_t}{\rho_b}$$

Table No.10: Hausner's ratio as an indication of powder flow properties

| Values | Comments |
|---|---|
| Less than 1.25 | Good flow |
| Greater than 1.5 | Poor flow |
| Between 1.25-1.5 | Addition of glidant normally improves flow |

## DESCRIPTION OF TECHNIQUES USED FOR IMMEDIATE RELEASE PREPARATION

### 3.8 Formulation of Oro-dispersible Tablet

Compression step: The obtained product mixed with drug, superdisintegrants, and sweetner, lubricant and glidant. It was obtained uniform particle size. Passed through mesh 40# ASTM hence finally compressed into tablet by keeping appropriate hardness. Hardness for oro-dispersible tablet is always kept low than conventional tablet in order to meet the minimum disintegration time but also friability within the limit.

## 4. EVALUATION OF PREPARED ORO-DISPERSIBLE TABLETS

The evaluation tablet's properties are important in the determination of product quality. There are various standards that have been set in the various pharmacopoeias regarding the quality of pharmaceutical tablets. These include the diameter, size, shape, thickness, weight, hardness, disintegration and dissolution characteristics. The diameters and shape depend on the die and punches selected for the compression of tablets. The following standards or quality control tests were carried out on compressed tablets of all formulation batches.

### 4.1 Appearance

The general appearance of a tablet involves tablet's size, shape, color, odor, taste, surface texture, consistency, and presence of any identifying markings.

### 4.2 Thickness and Diameter

The thickness and diameter of individual tablets was measured using Vernier calliper. Tablet thickness should be controlled within ± 5% variation of a standard value.

### 4.3 Weight Variation

Twenty tablets were selected at a random and average weight was determined. Then individual tablets were weighed and was compared with average weight. According to I.P., not more than two of individual weights deviate from the average weight by more than stated % and none deviates by more than twice that relevant percentage.

### 4.4 Hardness

The limit of crushing strength for an Immediate Release is usually kept low so as to facilitate early disintegration in the mouth. Tablet hardness means its diametric crushing strength (Fc) was measured by using Monsanto tablet hardness tester or Pfizer.

### 4.5 Friability

Friction and shock are the forces that most often cause tablets to chip, cap or break. The friability test is closely related to tablet hardness and is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. Friability of the tablets was determined using Roche Friabilator (LabinLI –FT-1). Usually it should be below 1%, an indication of good mechanical resistance of tablets. Pre-weighed sample of tablets was placed in the friabilator and subjected to 100 revolutions (25 rpm). The tablets were de-dusted using a soft muslin cloth and reweighed.

The friability (f) is given by the formula,

$$f = (1 - \frac{W_o}{W}) \times 100$$

Where, Wo = weight of the tablets before the test

W = weight of the tablets after the test.

Usually, it should be below 1%, an indication of good mechanical resistance of tablets.

### 4.6 In vitro Disintegration Time

The disintegration time of Oro-dispersible tablets was determined in conventional disintegration test apparatus (Electrolab ED-2-L) in accordance with the official European Pharmacopoeia monograph 'Oro-dispersible tablets' stating a maximum disintegration time of 3 min. Disintegration or more specifically dispersion times were measured in 900 ml purified water according to the I.P. method without using disc at room temperature (25℃ ± 2℃).

### 4.7 Water Absorption Ratio / Wetting Time

Wetting time of dosage form is related with the contact angle. Wetting time of the Oro-dispersible tablet is another important parameter, which needs to be assessed to give an insight into capillarity and subsequently the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. Wetting time of dosage form is related with the contact angle. A lower wetting time implies a quicker disintegration of the tablet.

A piece of tissue paper folded twice was placed in a small petri dish containing 6 ml of water. A tablet was put on the tissue paper and allowed to wet completely. The wetted tablet was then reweighed. Water absorption ratio, R was determined using following equation,

$$R = 100 \times \frac{W_a - W_b}{W_b}$$

Where, Wa= weight of tablet after water absorption and

Wb= weight of tablet before water absorption.

### 4.8 Dissolution Study for Trazodone HCl Immediate Release

With the help of USP type II apparatus, dissolution studies were carried out at 50 rpm. The dissolution media used for this study was 0.1 N hydrochloric acid. The temperature was retained at 37±2°°C. At specific time interval, aliquots of dissolution media were withdrawn and filtered. Moreover, it was restored with the same amount of fresh dissolution media. Further, the filtered solution was observed spectrometrically at 278 nm to find out the drug content. For all designed formulations, the dissolution study was carried and the results were compared with conventional and marketed tablet Apotex.

## 5. DRUG RELEASE KINETIC STUDY

To analyse the mechanism of release and release rate kinetics of the dosage form, the data obtained were fitted into Zero order,First order, Higuchi matrix, Korsrmeyer Peppas model.

The release kinetic studies were performed on formulation batch. Based on the R-value, the best-fit model was selected. The linearity of the plots was obtained from the value of regression coefficient (R2). The model with the highest linearity (R value approaches unity) was chosen as the best-fit kinetic model.

**5.1 Zero order kinetics:**

Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly, assuming that the area does not change and no equilibrium conditions are obtained can be represented by the following equation,

$$Qt = Qo + Ko\ t$$

Where,

Qt is amount of drug dissolved in time t, Qo is initial amount of the drug in the solution and K o is zero order release constant.

**5.2 Immediate Release First order kinetics:**

To study the First order release rate kinetics, the release rate data were fitted to the following equation,

$$Log\ Qt = log\ Qo + K1\ t/2.303$$

Where,

Qt is the amount of drug released in time t, Qo is the initial amount of drug in the solution and K1 is the First order release constant.

**5.3 Higuchi model:**

Higuchi developed several theoretical models to study the release of water soluble and low soluble drugs incorporated in semisolids and/or solid matrices. Mathematical expressions were obtained for drug particles dispersed in a uniform matrix behaving as the diffusion media. And the equation is,

$$Qt = KH \cdot t1/2$$

Where,

Qt is amount of drug released in time t, KH is Higuchi dissolution constant.

**5.4 Korsmeyer and Peppas release model:**

To study this model the release rate data are fitted to the following equation,

$$Mt / M\infty = K \cdot tn$$

Where,

Mt / M∞ is the fraction of drug release, K is the release constant, t is the release time and n is the diffusional coefficient for the drug release that is dependent on the shape of the matrix dosage form.

Table No.11: Interpretation of Diffusion Release Mechanisms from Polymeric Matrix

| Release exponent (n) | Drug transport Rate as a function mechanism |
|---|---|
| 0.5 | Fickian diffusion |
| 0.5< n< 1.0 | Non- Fickian or Anomalous transport |
| 1.0 | Case-II transport |
| Higher than 1.0 | Super Case-II transport |

**6. STABILITY STUDY**

Stability of a drug has been defined as the ability of a particular formulation, in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications.The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of Immediate Release environmental factors such as temperature, humidity and light and enables recommended storage conditions, re-test periods and shelf lives to be established.Optimized batch was selected for stability study.

Table No.12: Storage conditions as per ICH guidelines

| Sr. No. | Study | Condition | Duration |
|---|---|---|---|
| 1 | Long term Study | 25ºC ± 2 ºC/60 % ± 5% RH OR 30ºC ± 2 ºC/65% ± 5% RH | 12 months |
| 2 | Intermediate Study | 30ºC ± 2 ºC/65% ± 5% RH | 6 months |
| 3 | Accelerated Study | 40ºC ± 2 ºC/75% ± 5% RH | 6 months |

The Trazodone HCl tablet batch stored at temperature of 40oC ± 2°C / 75 % RH ± 5 % RH. The products were stored for a period of 3 months in the above-mentioned conditions. The product was analysed for the changes in physical appearance, weight variation, friability, hardness, In-vitro drug release after intervals of one month up to three months.

## RESULT AND DISCUSSION

**7. Preformulation study**

Preformulation testing is the First step in the rationale development of dosage forms. Preformulation testing encompasses all studies with drug in order to produce useful information for subsequent formulation of stable and suitable dosage form.

**7.1 Characterization of drug (Trazodone Hydrochloride)**

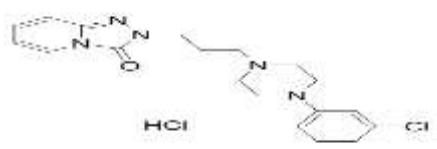
The characterization of drug is necessary for identification and purity of drug. In characterization of drug different physical, chemical and spectroscopic tests were performed which are given below. .

**7.2 Identification test**

**7.2.1 Immediate Release IR spectroscopy**

Immediate Release IR spectra interpretation study was performed for the identification of Trazodone HCl

| Wave numbers ($cm^{-1}$) | Groups present |
|---|---|
| 1731.28 | C=O Stretch |
| 2966.85 | N-H Bending |
| 3315.82 | N-H Bending |
| 3677.68 | O-H Stretch |



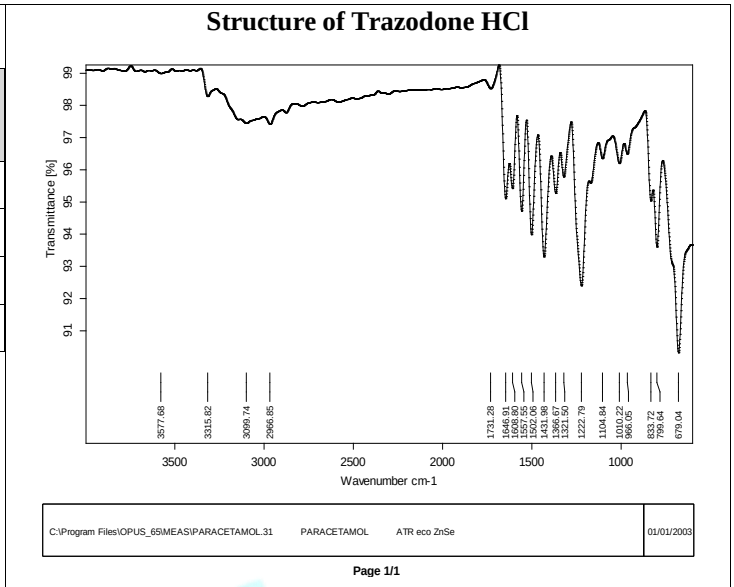




Figure No. 1: Immediate Release spectra interpretation of Trazodone HCl

FT-Immediate Release study is important for determination of functional groups present in structure of sample. The Immediate Release spectrum of the pure Trazodone HCl sample was recorded by FT-Immediate Release
spectrometer as shown in table 7.1. The major peaks observed and corresponding functional groups are also given in table7.1.

**7.3 UV spectroscopy**

**7.3.1 Determination of absorption maxima**

The absorption maxima of Trazodone HCl in water was determined using double beam UV spectrophotometer. The λmaxof Trazodone HCl in pH 1.2 was found to be 278 nm. The λmax for Trazodone HCl of 10 ppm solution is shown in following figure. (Fig. 2)

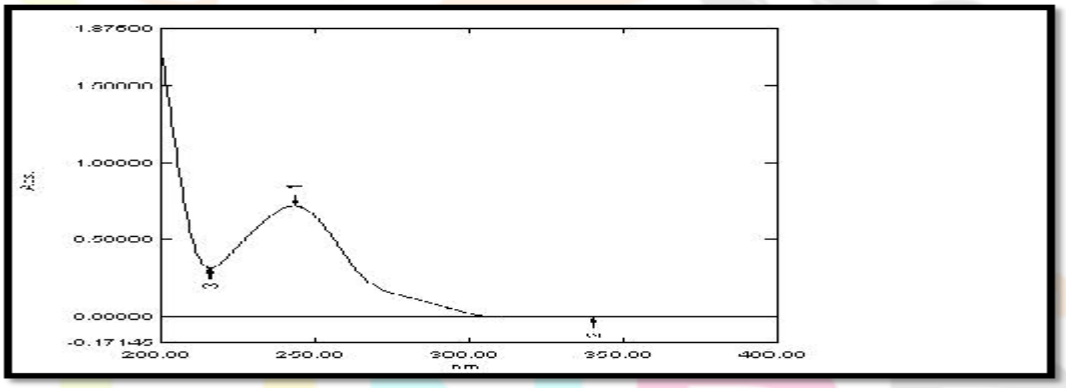



Figure No.2: UV spectrum of Trazodone Hydrochloride

Table No.13: Absorbance at different concentrations

| Sr. No. | Concentration (µg/ml) | Absorbance (278 nm) |
|---|---|---|
| 1 | 10 | 0.070 |
| 2 | 20 | 0.135 |
| 3 | 30 | 0.198 |
| 4 | 40 | 0.265 |
| 5 | 50 | 0.333 |
| 6 | 60 | 0.398 |
| 7 | 70 | 0.444 |

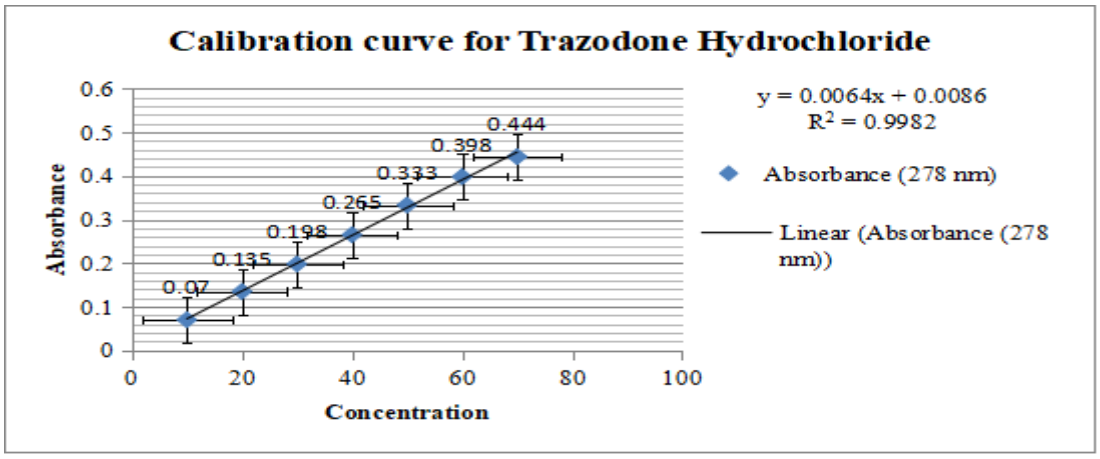



Figure No.3: Calibration curve of Trazodone Hydrochloride

The standard calibration curve of 10-70µg/ml.The observed absorbance showed in the above figure. (Fig.3) and regression coefficient was 0.998.

**7.4 Physicochemical study**

**7.4.1 Organoleptic characterization**

The organoleptic properties determined by the senses including sight, smell & touch. Paracetamol was found to be white crystalline powder. The organoleptic properties of Trazodone HCl were found to be same as that specified in the standards.

**7.4.2 Solubility study**

The solubility study of Trazodone HCl was carried out. The Trazodone HCl was found to be freely Soluble in ethanol, Acetone, sparingly soluble in water etc and it was concluded that it passes solubility test.

**7.4.3 Melting point determination**

The melting point of Trazodone HCl was found to be 87ºC and standard melting point was 75-87ºC.

**7.4.4 Loss on drying**

The loss on drying for Trazodone HCl sample was found to be 0.2% which was within the limit of IP specification that is NMT 0.5%.

**7.5 Characterization of excipients**

Before going for formulation development study, it is necessary to check the quality of raw materials so each excipient characterized for organoleptic behaviour, and Immediate Release spectroscopy.

**7.6 Organoleptic Characterization**

All the observations were summarized in following table. (Table No. 14)

Table No.14: Organoleptic characterization of excipients

| Excipient | Observation | Standard |
|---|---|---|
| Aerosil 200 Pharma | Aerosil 200 Pharma was found to be a white to creamy-white, finely divided, free flowing, hygroscopic powder. | Aerosil 200 Pharma occurs as a white to creamy-white, finely divided; free flowing, practically tasteless, odorless or nearly odorless, hygroscopic powder. |
| Sodium Starch Glycolate | Sodium starch glycolate is a white to off-white, odorless, tasteless, free-flowing powder. | Sodium starch glycolate is a white to off-white, odorless, Tasteless, free-flowing powder. |
| MCC 302 | MCC 302 was found to beawhite, odorless, crystalline powder | MCC 302 occurs as a white, odorless, crystalline powder or free-flowing granules |
| Xylitol | Xylitol was found to be a white, granular solid comprising crystalline, equidimensional particle | Xylitol occurs as a white, granular solid comprising crystalline, equidimensional particle |
| Magnesium Stearate | Magnesium stearate was found to be very fine, light white, milled, impalpable powder of low bulk density, having a faint odor of stearic acid. The powder is greasy to the touch and readily adheres to the skin. | Magnesium stearate occurs as a very fine, light white, precipitated or milled, impalpable powder of low bulk density, having a faint odor of stearic acid and a characteristic taste. The powder is greasy to the touch and readily adheres to the skin. |
| Lactose Anhydrous | Lactose Anhydrous is a white to off-white, odorless,tasteless, free-flowing powder. | Lactose Anhydrous is a white to off-white, odorless, Tasteless, free-flowing powder |

**8. IR study**

IR pectra interpretation study was performed for the identification of all the excipients. The characteristics peaks of all the excipients were summarized in table. The Immediate Release spectra of the all-excipients sample have shown below.

**Mannitol**

| Wavenumber ($cm^{-1}$) | Groups present |
|---|---|
| 1291.12 | 0-H Bending |
| 1072.66 | C-C stretching |
| 2971.48 | C-H stretching |
| 865.O8 | C-H Rocking |

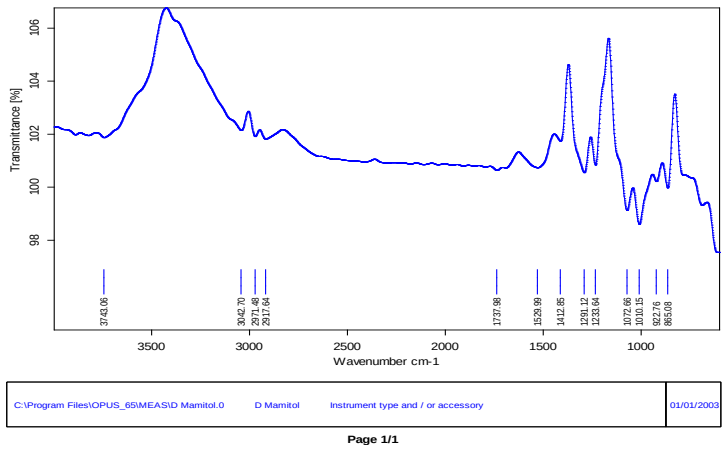
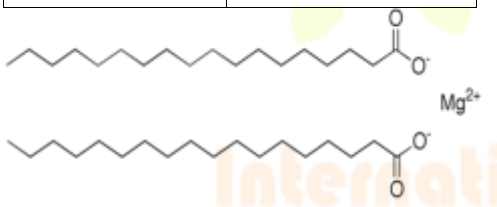



Figure No. 4: Immediate Release spectra interpretation of MCC 302

**Magnesium Stearate**

| Wave number ($cm^{-1}$) | Groups present |
|---|---|
| 1534.66 | C=O Stretch |
| 2914.77 | C-H Stretch |
| 1464.97 | C-H Bending |
| 3040.74 | O-H Stretch |



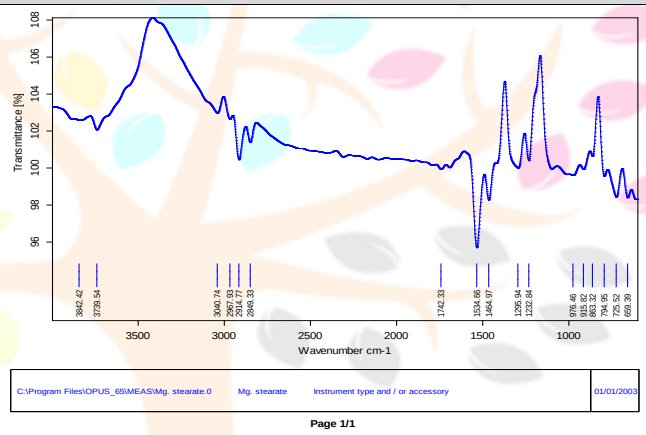




Figure No. 5: Immediate Release spectra interpretation of Magnesium Stearate

## 9. Compatibility study

Compatibility studies for Paracetamol with all excipients were carried out prior to formulation of tablet.

Table No. 15: Compatibility study after 14 days

| Physical mixture | Observation | | | |
|---|---|---|---|---|
| | Color change | Cake formation | Liquification | Gas formation |
| Trazodone HCl l | No | No | No | No |
| Drug+ MCC 302 | No | No | No | No |
| Drug+ Sodium Starch Glycolate | No | No | No | No |
| Drug+ Lactose anhydrous | No | No | No | No |
| Drug+ Xylitol | No | No | No | No |
| Drug+ Aerosil 200 Pharma | No | No | No | No |
| Drug+ Magnesium Stearate | No | No | No | No |

A) Before B) After

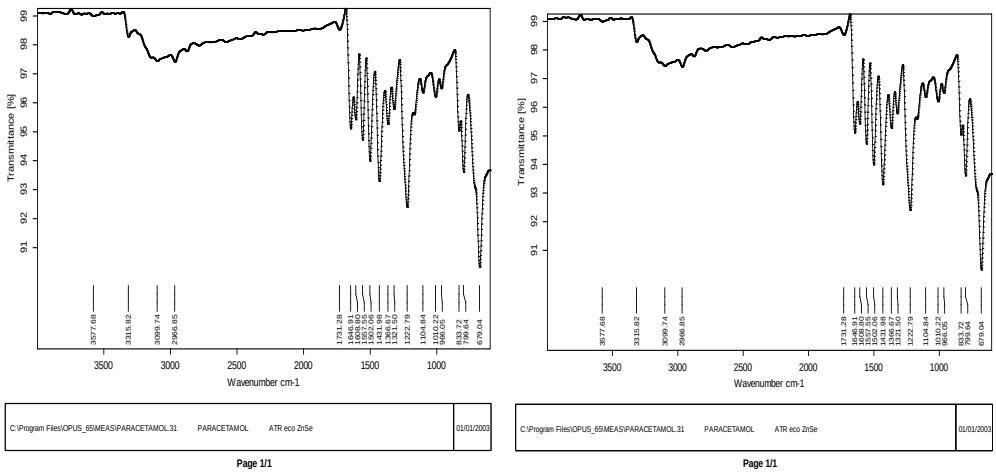



Figure No. 6: Drug (Trazodone HCl)

A) Before B) After

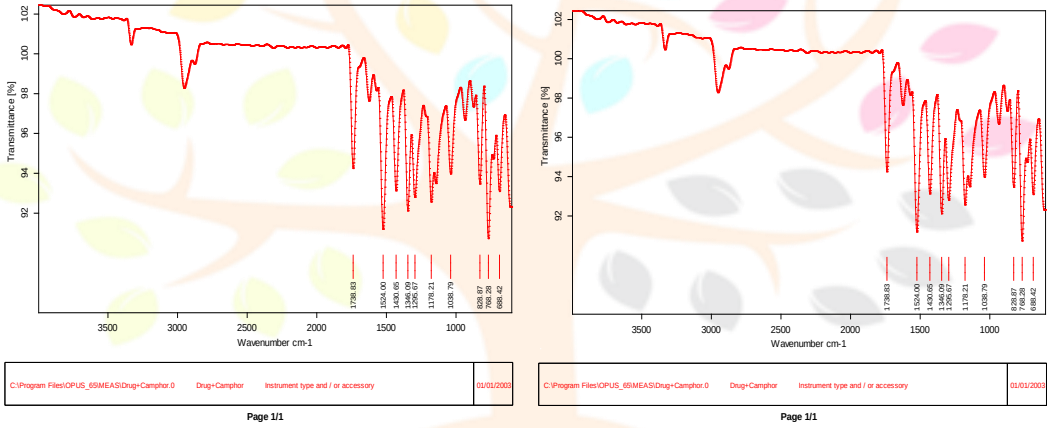



Figure No. 7: Drug + MCC 302

A) Before B) After

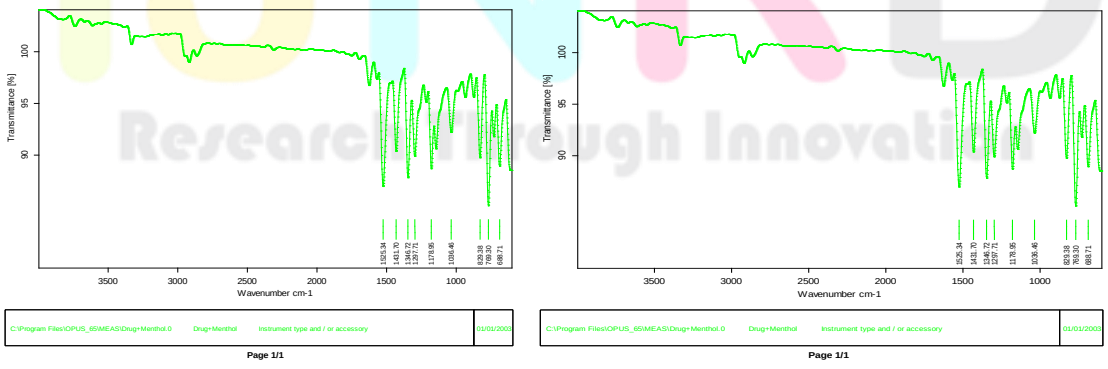



Figure No. 8: Drug + Sodium Starch Glycolate

A) Before B) After

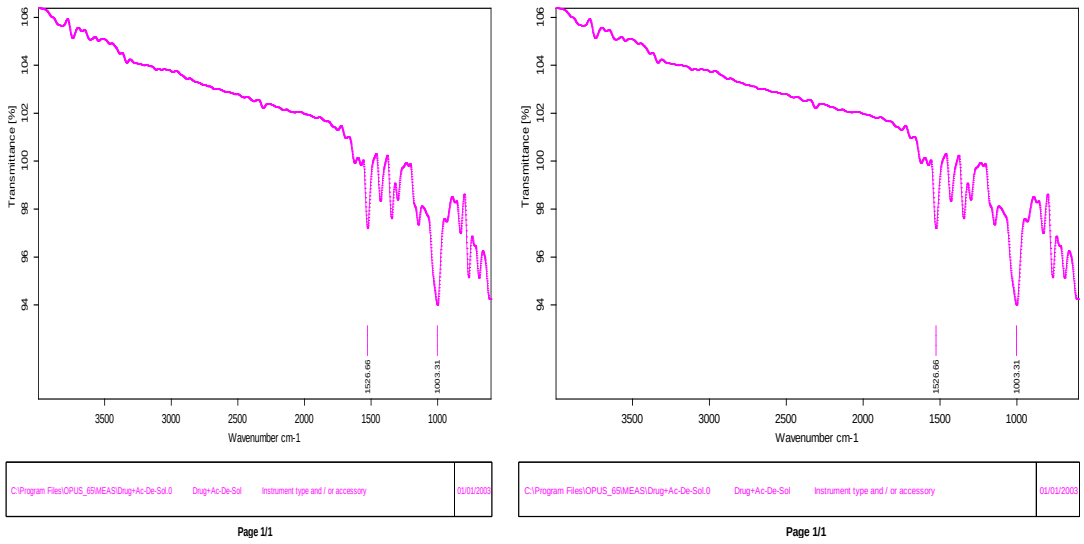



Figure No. 9: Drug + Lactose anhydrous

A) Before B) After

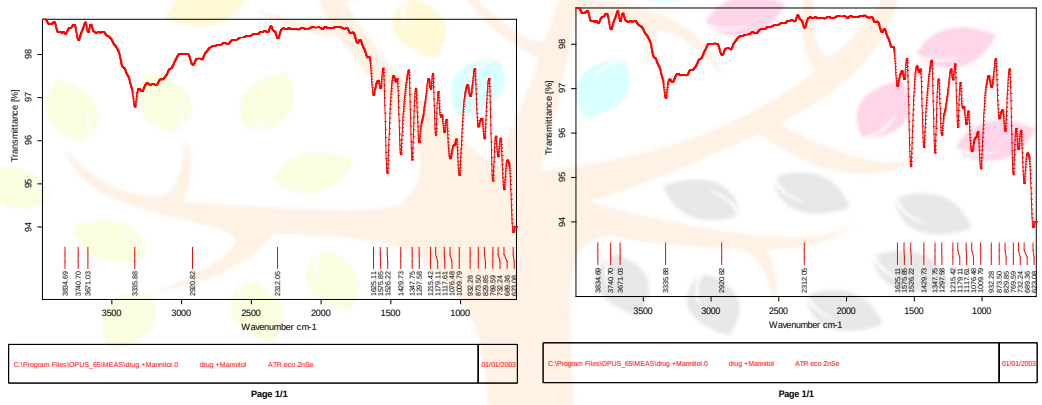



Figure No. 10: Drug + Aerosil 200 Pharma

A) Before B) After

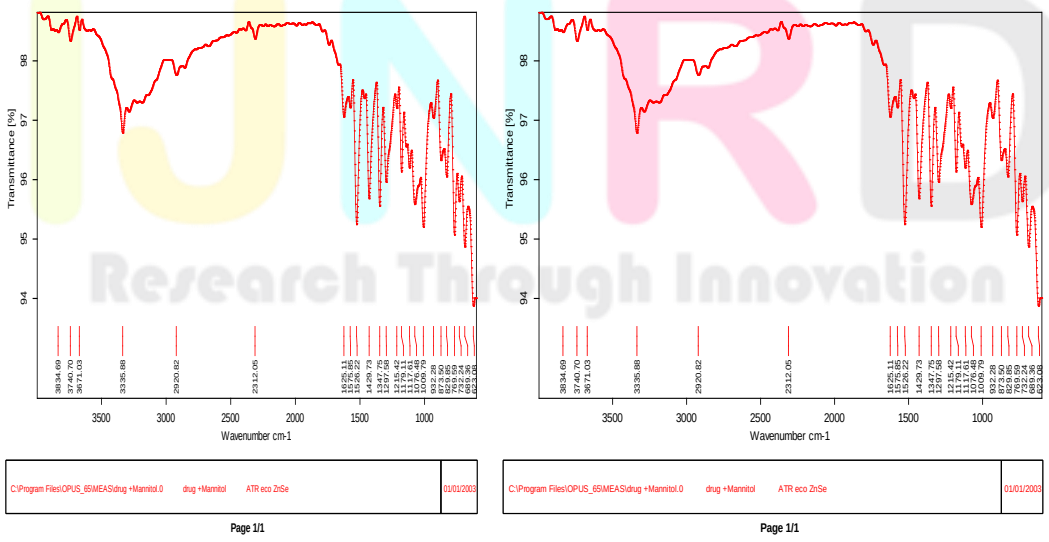



Figure No. 11: Drug+ Xylitol

A) Before B) After

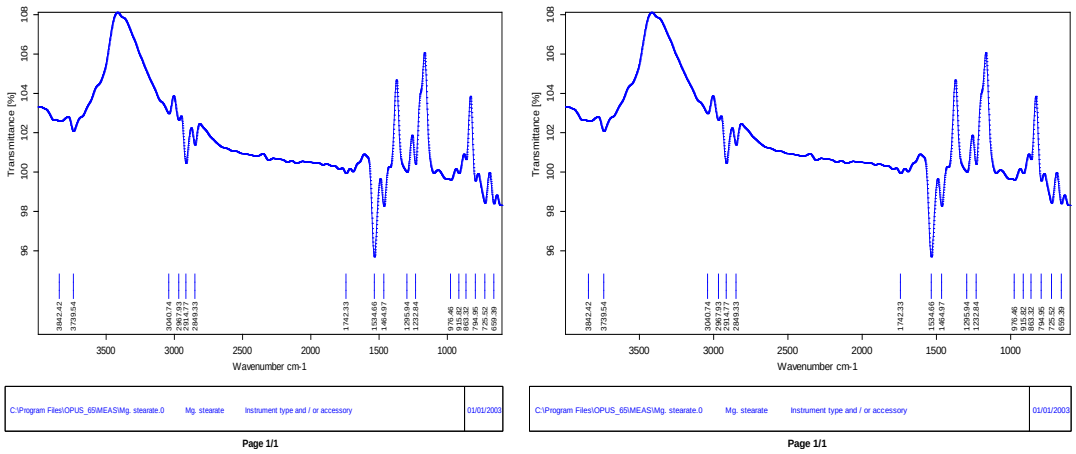



Figure No. 12: Drug + Magnesium Stearate

**Significance:**

From above Immediate Release graphs could be seen that there is no change in the graphs of without moisture. It indicates that there is no interaction between drug and excipients hence drug is compatible with all excipients and also excipients are compatible with drug and hence can be used for further study

**10. Preformulation study for blend materials.**

All the batches were found to be a Immediate Release flow property. All the formulations were shown reproducible result in terms of flow property of powders. (Table No.16)

Table No. 16: Precompression characteristics of formulations

| Code | Bulk Density gm/ml | Tap Density gm/ml | Cars,s Index (%) | Hosnors Ratio | Angle of Repose |
|---|---|---|---|---|---|
| F1 | 0.54 | 0.63 | 21.02 | 1.25 | 34.8 |
| F2 | 0.52 | 0.64 | 24.21 | 1.17 | 35.2 |
| F3 | 0.45 | 0.57 | 13.04 | 1.16 | 33.1 |
| F4 | 0.48 | 0.59 | 14.72 | 1.11 | 32.4 |
| F5 | 0.50 | 0.57 | 12.79 | 1.15 | 32.5 |
| F6 | 0.51 | 0.62 | 13.11 | 1.15 | 31.9 |
| F7 | 0.49 | 0.59 | 18.90 | 1.11 | 30.3 |
| F8 | 0.55 | 0.62 | 17.11 | 1.12 | 32.1 |
| F9 | 0.57 | 0.67 | 18.69 | 1.23 | 31.8 |

**10.1 Post compression characterization (Prepared Immediate Release)**

For the five batches the evaluation parameters for Hardness, friability, and disintegration time.

Table No. 17: Post-compression before sublimation characteristics of formulations

| Code | Hardness (Kg / cm2) | Friability (%) | Thickness (mm) | Disintegration time (sec) | Weight variation (average weight) (mg) | Wetting time (sec) |
|---|---|---|---|---|---|---|
| F1 | 3.6 | 0.40 | 2.8 | 42 | 1.06 | 3.5 |
| F2 | 3.9 | 0.44 | 2.9 | 37 | 1.04 | 3.1 |
| F3 | 3.9 | 0.46 | 2.7 | 32 | 1.01 | 2.7 |
| F4 | 4.3 | 0.40 | 2.8 | 35 | 0.99 | 2.6 |
| F5 | 4.0 | 0.47 | 2.6 | 27 | 1.06 | 2.2 |
| F6 | 3.7 | 0.43 | 2.7 | 21 | 1.05 | 1.7 |
| F7 | 3.6 | 0.42 | 2.7 | 69 | 0.98 | 4.2 |
| F8 | 3.8 | 0.43 | 2.9 | 53 | 1.02 | 3.9 |
| F9 | 3.8 | 0.45 | 2.7 | 46 | 0.99 | 3.4 |

## DISCUSSION

It was seen that the formulation of oro-dispersible Traodone HCl tablet by Immediate Release Compression technique was done. And taste masking was done properly. The taste masking was evaluated by the solubility testing.
For this testing the organic solvent i.e. Acetone was taken, and the tablet was dissolved in acetone and then identification test was done by the UV Spectrophotometry. The above solution observed under UV and result was observed that the absorbance at 278 nm was not found. Above test shows that the taste masking was properly done.

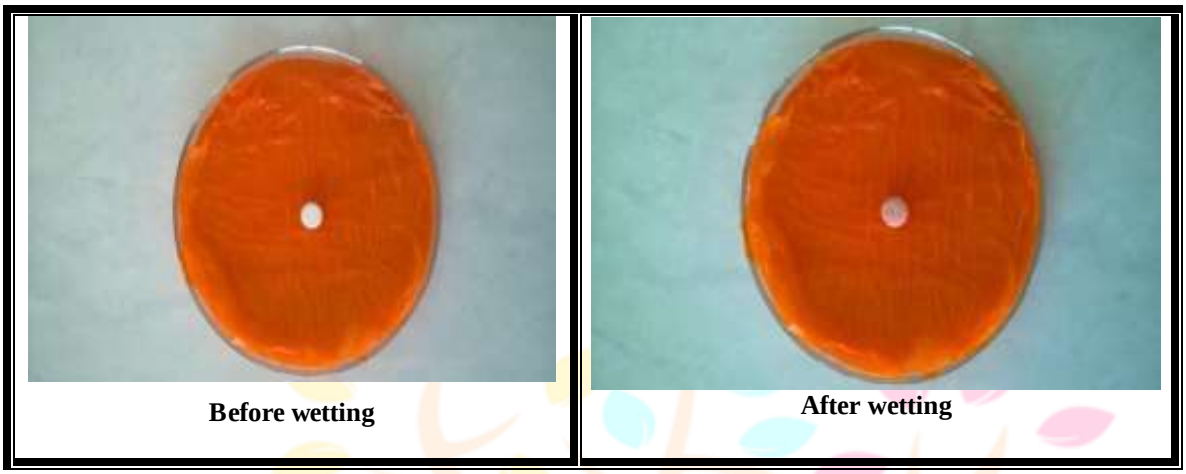



Figure No. 13: Wettability Study of Tablets (Before and After) Wetting time of batch F5

The result of dissolution study was showed in the following table No.18

Table No. 18: Dissolution profile for prepared Immediate Release formulations

| Sr. No. | Time (Min) | Cumulative % Drug Release | | | | |
|---|---|---|---|---|---|---|
| | | F1 | F2 | F3 | F4 | F5 |
| 1 | 5 | 36.23 | 28.12 | 19.52 | 29.56 | 34.22 |
| 2 | 10 | 52.36 | 43.50 | 28.12 | 33.65 | 48.25 |
| 3 | 15 | 72.11 | 48.25 | 51.25 | 58.10 | 56.11 |
| 4 | 20 | 84.33 | 75.61 | 63.75 | 82.85 | 72.21 |
| 5 | 25 | 90.02 | 93.25 | 90.87 | 91.87 | 85.17 |
| 6 | 30 | 94.75 | 97.50 | 96.28 | 94.64 | 98.42 |

Table No. 19: Comparison data of drug release Profile

| Sr. No. | Time (Min) | Cumulative % Drug Release | | | |
|---|---|---|---|---|---|
| | | F6 | F7 | F8 | F9 |
| 1 | 5 | 45.22 | 47.38 | 14.23 | 39.55 |
| 2 | 10 | 62.95 | 69.20 | 28.12 | 62.95 |
| 3 | 15 | 69.20 | 72.90 | 51.25 | 69.20 |
| 4 | 20 | 85.17 | 85.17 | 63.75 | 82.85 |
| 5 | 25 | 93.87 | 96.28 | 84.02 | 96.28 |
| 6 | 30 | 99.75 | 99.25 | 93.05 | 99.23 |

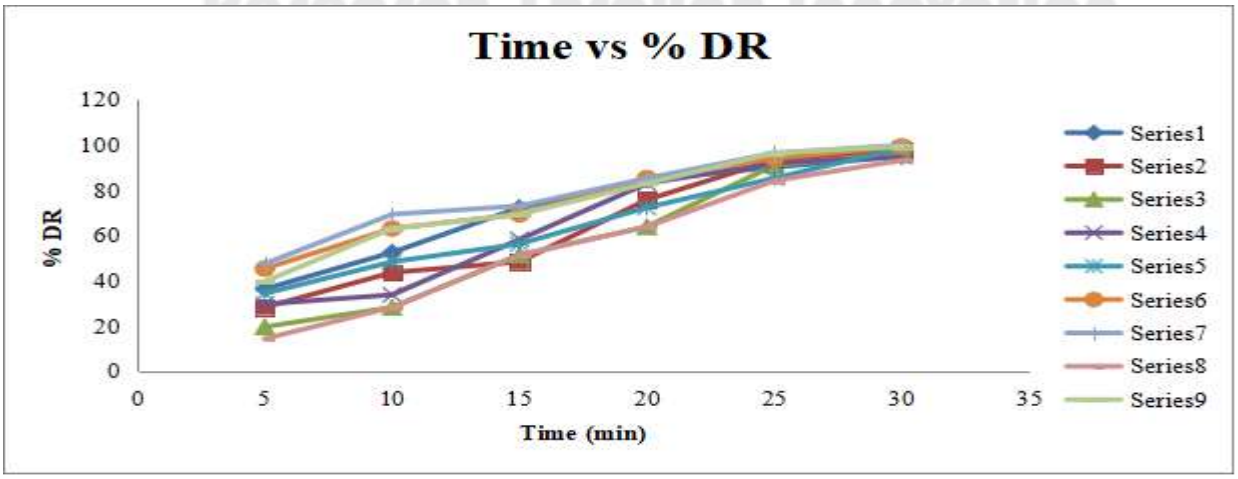


Figure No. 14: Comparison of drug release Profile

α) After studying drug release it was concluded that faster disintegration has a Immediate release effect on dissolution.
β) Tablets containing the physical mixtures of SSG and microcrystalline cellulose 302 with showed faster drug release which might be attributed due to increased in porosity as compare to marketed one.

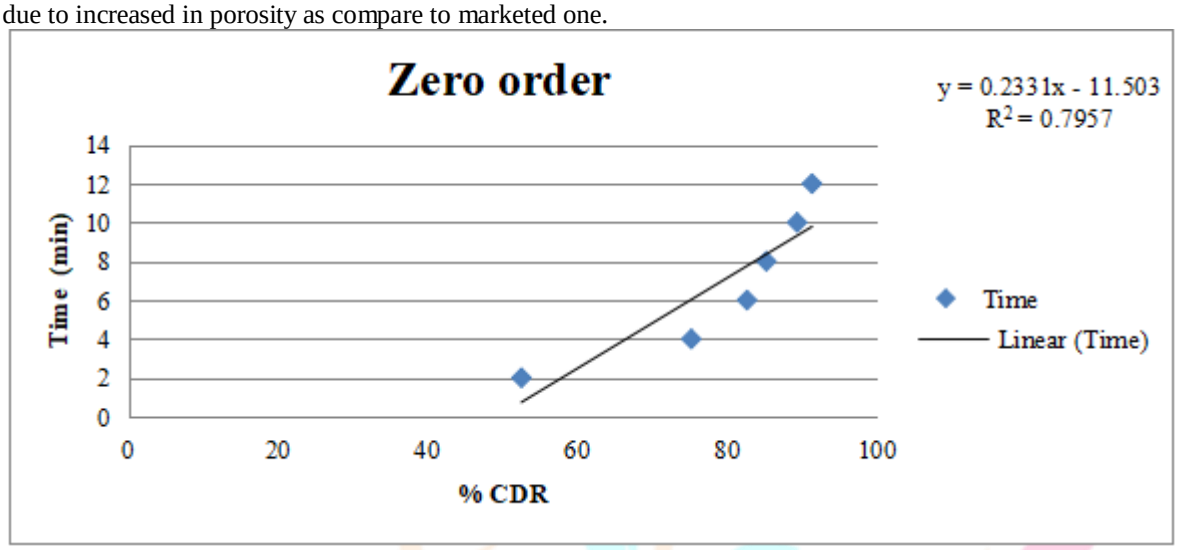



Figure No. 15: Release kinetics of zero order model

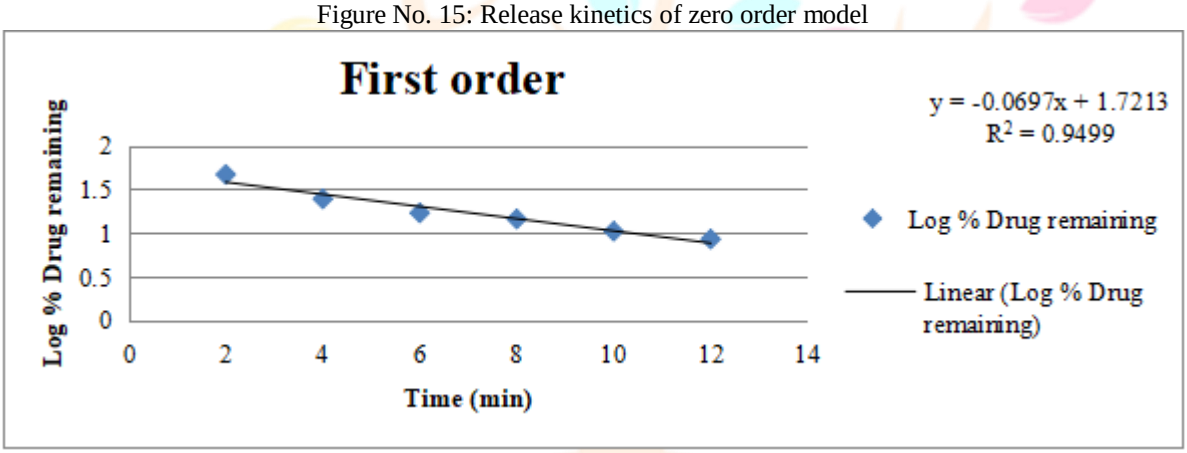



Figure No. 16: Release kinetics of fImmediate Releasest order model

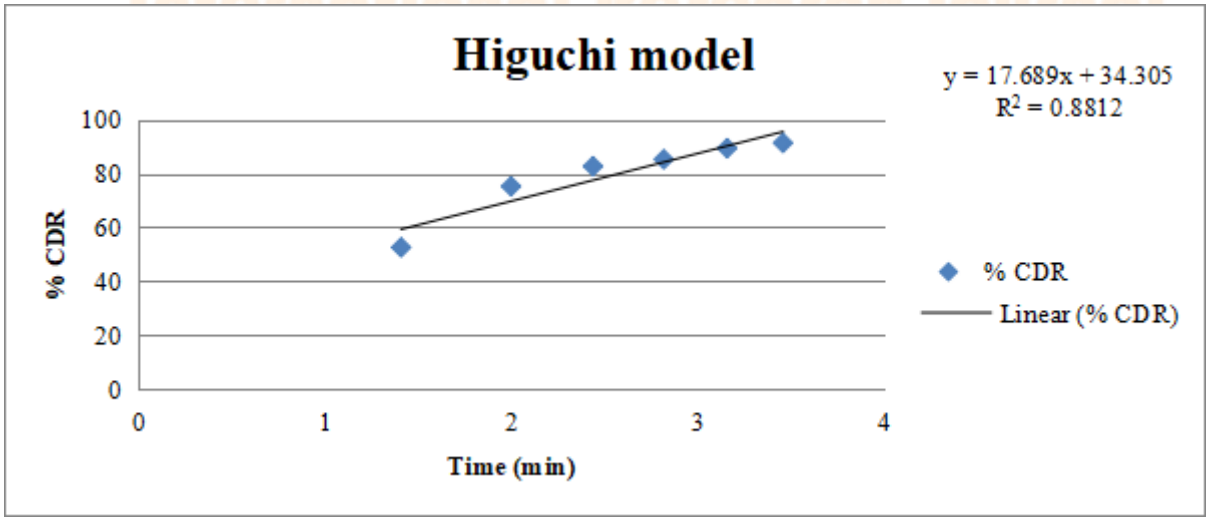



Figure No. 17: Release kinetics of Higuchi model

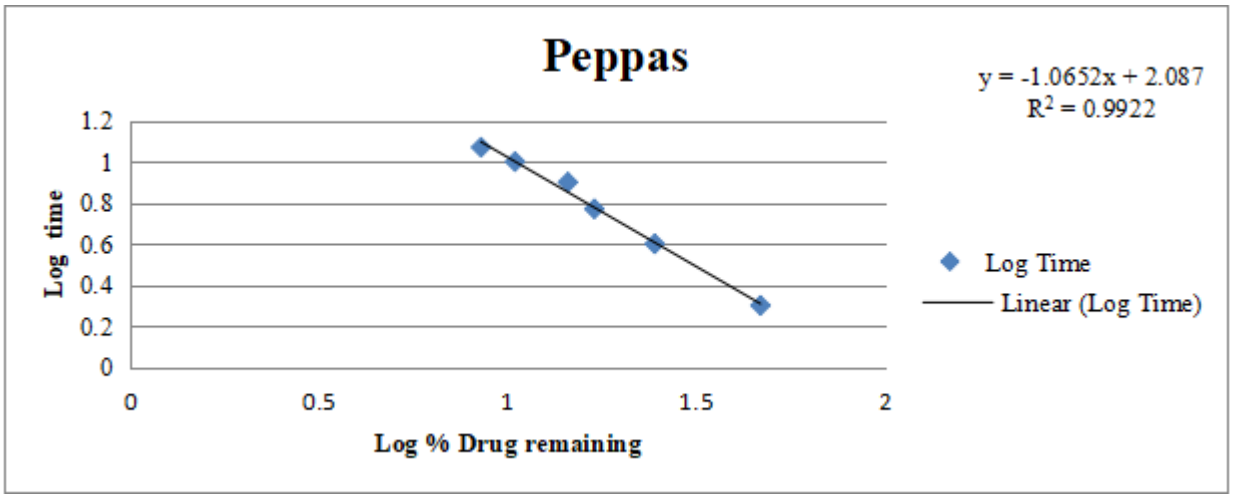



Figure No. 18: Release kinetics of peppas model

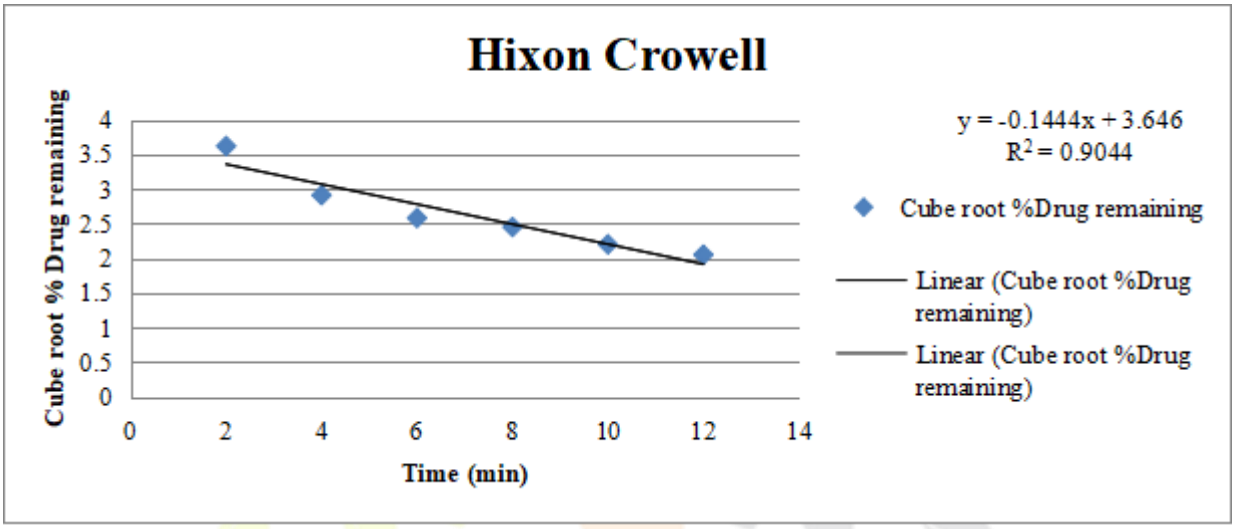



Figure No. 19: Release kinetics of Hixon crowell model

Table No. 20: Regression coefficients of all Release kinetic models

| Regression coefficients ($r^2$) | | | | |
|---|---|---|---|---|
| **Zero-order** | **FImmediate Releasest-order** | **Higuchi model** | **Hixson Crowell** | **Peppas model** |
| 0.795 | 0.949 | 0.881 | 0.904 | 0.992 |

**Justification:** Drug release kinetics study indicates that drug release from tablet follows Peppas model according to regression coefficients ($r^2$) v

## SUMMARY AND CONCLUSION

Orally Disintegrating tablets (Immediate Releases) emerged with an objective to improve patient's compliance. These dosage forms rapidly disintegrate and/or dissolve to release the drug as soon as they come in contact with saliva, thus obviating the need for water during administration. The aim of the present work is to formulate, develop and evaluate Trazodone HCl Immediate Release using diluents and Direct compression technique. Reason behind using this both techniques was to maintain both hardness and disintegrating time of the dosage form so that it can withstand its mechanical strength while transportation. Antidepressant drug Trazodone HCl was selected for formulating oral dispersible tablet because the patients suffering from severe vomiting would get quick onset of action.

- Immediate Release spectra revealed that, the drug sample was pure.There was no interaction between excipients and drug. Excipients selected for Immediate Releases are compatible with Trazodone HCl. The Immediate Release analysis indicates that there was no drug-excipients interaction. Preformulation studies for both drug and excipients were determined. Preliminary trails for super disintegrants, subliming agents and diluents were performed. From preliminary trails SSG as superdisintegrant and MCC were selected with Optimized ratio.The in-vitro disintegration study reveals that Immediate Release disintegrates within 27 seconds which is good indication for its rapid drug delivery. The in-vitro dissolution study shows the drug release More than 95% in 30 min. It was observed from that the MCC 302 crystals are fine and uniformly distributed in the microcrystalline matrix in compressed form compared to physical mixture of the same combination this mechanism helps to improve compressibility and disintegrating time.The fast disintegration may be due to the partial amorphization and formation of submicron particles of MCC 302. And hardness was maintained due to typical plastically deformed characteristics of MCC.Finally it was concluded that using co processed Lactose and MCC improved compressibility of the tablet to with stand its mechanical strength and incorporation.

**SELF INTRODUCTION BIODATA**

**Dr. ( H.C.) Santosh Dattu Navale, Scientist Pharmaceutical R & D , Polymer Scientist, State Intelligence Agents Director of Maharashtra, NAAC & IHRCCC Officer, MMA- Martial Artist, Break Dancer**
**(Magic Bullet Intercepting Fist Martial Arts & Nun Chucku Golden Mask)**

I Dr. (h.c.) Santosh Dattu Navale, I enclose my Biodata of Introduction as a fImmediate Releasest step in exploring the possibilities of achievements. This will help me in getting good exposure to the highly sophisticated ambience and understanding the anticipation and theoretical, practical aspects. I am professionally scientist in Polymer as well as Pharmaceutical R & D Lab, M Pharmacy Post Graduate in Pharmaceutics, Savitribai Phule Pune University FImmediate Releasest Class with Distinction, hence also qualified competitive exam like GPAT, NIPER, Attempted and qualified MPSC & UPSC, IQ Test meanwhile also doing Social Service Work, Corona Warrior as Pharmaceutical field, part time work in NGO of (NCIA) National Crime Intelligence Agency designated as Intelligence Agent, Executive and Information Officer, NCIA STATE INTELLIGENCE DIRECTOR, MAHARASHTRA, NGO (IHRCCC) International Human Rights and Crime Control Council designated as Officer. Self Defense and Martial Arts (MMA), own style of Break Dancing as well as included my own style of Magic Bullet Intercepting Fist. I have also published more than 25 Pharmaceuticals Review, Research articles in International Journal with and 3 Doctorates (Hon.) Honoris Causa University, more than 50 Awards winner national as well as international platform hence also World Record holder in Magic Book of World Record, Indian Book of World Record, London Book of World Record, Champion Book of World Record, Web Book of World Records, USA Book of World Record, Magic Bullets Intercepting Fist Novel Advance technique also Published in International Journal of IJNRD and IPR of Indian Patent and many more. The draft of patent prepared and accepted for review board intellectual property rights India. The pharmaceutical company was founded to achieve newer heights in pharmaceutical technologies and science. Team of over scientists spearhead pharmaceutical development programs of world's major pharmaceutical markets. We pride ourselves in solving problems for R & D and manufacturing. Kindly Referred and find enclosed my PROFESSIONAL, DEFENSE AND SOCIAL WORK PROFILE INTRODUCTION.

**NAMED REVIEW & RESEARCH PAPER PUBLICATIONS ON**

1. Review paper publication in **World Journal of pharmaceutical Research entitled** on **"**A REVIEW ON ORO-DISPERSIBLE TABLETS AND GENERAL CONSIDERATIONS". 2022
2. Review paper publication in **World Journal of pharmaceutical Research entitled** on **"**A REVIEW ON ORO-DISPERSIBLE TABLETS AND PATENTED TECHNOLOGY". 2022
3. Review paper publication in **American Journal of Pharma Tech Research entitled** on **"**A Review on New Drug Applications and General Considerations in Pharmaceutical Industry"**.** 2022
4. Review paper publication in **American Journal of Pharma Tech Research entitled** on **"**A Review on Nasal Drug Delivery System and General Considerations"**.** 2022
5. Research paper publication in **American Journal of Pharma Tech Research entitled** on **"**Particle engineering and spray drying process designing for solubility enhancement of LopinavImmediate Release".2021
6. Research paper publication in **World Journal of pharmaceutical Research entitled** on **"**THE EXPERIMENTAL DESIGN IN CHEMICAL ENGINEERING AND PHARMACEUTICAL INDUSTRY BY USING FLUID COATER & ROTA METER". 2021
7. Review paper publication in **American Journal of Pharma Tech Research entitled** on **"**Regulatory Authorities & Standards Institutions and Self Auditing Consideration in Pharmaceutical Industry"**.** 2021
8. Review paper publication in **American Journal of Pharma Tech Research entitled** on **"**A Fluidized Bed Polymer Coating Experiment and Practical Aspects of Design in Chemical Engineering and Pharma Industry"**.** 2021
9. Review paper publication in **American Journal of Pharma Tech Research entitled** on **"**A Review on Impurities Profiling in Pharmaceutical Analysis**".** 2018
10. Review paper publication in **American Journal of Pharma Tech Research entitled** on **"**A review on liposome: The cancer targeting aspects and effective upgraded vesicular systems**".**2017
11. Review paper publication in **'American Journal of Pharm Tech Research'** entitled on **"**Review on Topical Liposome: Drug Delivery through Skin". 2017
12. Review paper publication in **'American Journal of Pharm Tech Research'** entitled on "Study of effect of lyophilization on the physicochemical stability of liposome". 2017
13. Research paper publication in **'European Journal of biomedical and pharmaceutical Science '** entitled on "**FORMULATION AND IN-VITRO EVALUATION OF ORO-DISPERSIBLE TABLET OF ACETOAMINOPHEN MODEL DRUG BY USING SPRAY DRYING TECHNIQUE**". 2024

14. Research paper publication in **'International Journal of Novel Research and Development IJNRD '** entitled on **"MAGIC BULLET INTERCEPTING FIST NOVEL ADVANCE TECHNIQUE OF MARTIAL ARTS, 2024**

**AWARDS PARTICIPATED AND WINNINGS**

1. National Pride Award, trophy medal and certificate, socially point foundation, (regd. govt, of india), 2023
2. Pride of India Award, certificate, socially point foundation, (regd.), 2023
3. Mother Teresa Memorial Award, trophy medal and certificate, sahara charitable trust (regd. govt, of india),2023
4. Matrubhasha Sahitya Sanman, sangam academy and publication, 2023
5. Rashtriya Shikshak Ratna Sanman , navya foundation, 2023
6. Rashtriiya Pratishtha Puraskar, Award, trophy medal and certificate worthy wellness foundation, (regd. govt, of india ),2023
7. Rabindranath Tagore Kala Vibhushan Award, participation certificate, 2023
8. Ncia Appreciation Certificate Intelligent Agent for corona warrior social service,2023
9. International Iconic Award, certificate of appreciation, social service, 2023
10. National Excellence Education Award, trophy, medal and certificate sahara charitable trust (regd. govt, of india),2023
11. Best Achievers Award,Reg. No. 8361, world magic book record, best social activist award, trophy, momento, gold medal and certificate, 2023
12. Brand Icon of the Year Award, trophy, medal and certificate, 2023
13. Dr. B. R. Ambedkar Ratna Award, trophy medal and certificate, sahara charitable trust (regd. govt, of india), 2023
14. Rastriya Danveer Samman, certificate, sahara charitable trust(regd.govt,of india), 2023
15. National Youth Icon Award, certificate, sahara charitable trust(regd. govt, of india), 2023
16. International Yog Bharti Award, certificate, sahara charitable trust(regd. govt, of india), 2023
17. National Service Award, sangam academy and publication, 2023
18. Mr. India, Kohinoor of the India Award, certificate, sahara charitable trust (regd. govt, of india), 2023
19. World Record, London Book of World Record, certificate, international (pharma nddr scientist, ncia-ihrccc officer, information officer, intelligence agent, philosopher, researcher, crime researcher & intercepting fist martial artist)london country 2023 ( two records professional& social service, the intercepting fist martial arts )
20. Gyan Uday Foundation, Indian Iconic Award, govt. of india, category of education, literature & social serviece 2023
21. India Star Independent Award, Star Book of Record, govt. of india, category of education, literature & social serviece 2023
22. NCIA Foundation, certificate of appointment, information officer, nashik 2023
23. Bahrtiya Gaurav Samman, the faImmediate Release vision foundtion, 2023
24. Dr.B.R. Ambedkar Inetrnational Award, world charity welfare foundation, certificate of excellence international, education & social service, 2023
25. International Human Rights and Crime Control Council, certificate of appreciation award, from IHRCCC, msme & niti aayog, 2024
26. Prestigious Doctors Award, certificate of appreciation, worthy wellness foundation, global award, 2024
27. Web World Record, official book of world record, certificate, international (pharma nddr scientist, ncia-ihrccc officer, information officer, intelligence agent, philosopher, researcher, crime researcher & intercepting fist martial artist) approved 2024
28. Indian Book of World Record, indian humatarian award, certificate from supreme coart of india, social activist may 2024
29. Rashtriya Prerna Award, startup siksha foundation , multiwork 2024
30. USA World Record, USA Book of World Record, certificate, international (pharma NDDR scientist, ncia-ihrccc officer, information officer, intelligence agent, philosopher, researcher, crime researcher & intercepting fist martial artist) USA country 2024
31. India Proud of Book Record, IBPR certificate, national (pharma NDDR scientist, NCIA-IHRCCC officer, information officer, intelligence agent, philosopher, researcher, crime researcher & intercepting fist martial artist) USA country 2024
32. Atheletics Book of World Record, international chaImmediate Releaseman, magic bullet intercepting fist of martial artist and golden mask nun chucku 2024
33. International Human World Record, certificate of excellence, pharma scientist and magic bullet intercepting fist martial artist 2024
34. International pride award, certificate of excellence, (pharma scientist, martial artist break dancer and state intelligence agent dImmediate Releaseector of Maharashtra) 2024
35. National Award, faImmediate Release vision foundation, certificate of achievement pharma scientist and state intelligence agent dImmediate Releaseector of Maharashtra 2024
36. Global Icon National Award, certificate of achievement, pharma scientist, martial artist and break dancer 2024
37. Indian Pride Award, , certificate of appreciation, pharma scientist and state intelligence agent dImmediate Releaseector of maharashtra 2024
38. Independence Day Hero Samman Award, certificate of achievement, pharma scientist, martial artist and social activist 2024
39. International Award, akhil bhartiya marvaadi gujrati manch and maharashtra sanskrutik dnyanpith, certificate, trophy and momento 2024
40. Champion Book of World Record, magic bullet intercepting fist mma & golden mask nun chucku, kota rajasthan, 2024
41. Treta Yug Foundation, Samman International Award, certificate, trophy and momento 2024

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None

**Conflict of interest**

None

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