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# Formulation Development and Evaluation of Mouth Dissolving Tablet of Thiocolchicoside

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## ABSTRACT

The present study was aimed to formulate and evaluate the Mouth dissolving tablet of Thiocolchicoside. Preliminary investigation of drug was carried out with different. Compatibility of drug with polymers was confirmed by FT-IR study. Tablet were prepared with superdisintegrants like Sodium starch glycolate, and other ingredients such as Mannitol, Lactose, Maltose. Sodium saccharide and Talc by Direct compression technique. It was observed that the results obtained after evaluation of (F2) formulations follows standards prescribed for Mouth dissolving tablets. The tablet was evaluated for various evaluation parameters such as. Weight Variation. Thickness. Hardness, Friability, wetting time, water absorption ratio, In-vitro Disintegration Time, in-Vitro drug release study, and uniformity of Content etc. Mouth dissolving tablet of optimized formulation (F2) having Mouth disintegration, better dissolution and all necessary parameter within the range. Formulation F2 shows the highest drug release upto 99.63%. Finally it is concluded that the drug release from the Mouth dissolving tablet was increased by using the increased concentration of superdisintegrant upto certain conc. After increase in cone. Of superdisintegrant leads to decrease disintegration in the buccal cavity. Increased systemic availability of drug will lead to quick onset of action, which is a prerequisite for analgesic activity.

***KEYWORDS:*** *Thicochicoside, Muscle relexant, MDT tablet, Direct compression method*

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## INTRODUCTION

Despite of tremendous innovations in drug delivery, the oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low cost therapy, self-medication, non-invasive method and ease of administration leading to high level of patient compliance. However, traditional tablets and capsules administered with a glass of water may be inconvenient or impractical.

To obviate the problems associated with conventional dosage forms, mouth dissolving tablets have been developed having good hardness, dose uniformity, easy administration and serves as the first choice of dosage form for paediatrics, geriatrics and travelling patients.

The technology is also referred to as fast disintegrating tablet, fast dispersing tablet, rapid dissolve tablet, rapid melt tablet, quick disintegrating tablet, and orally disintegrating tablet.

These are novel types of tablets that disintegrate/dissolve/disperse in saliva within few seconds. According to European Pharmacopoeia, the MDT should disperse/disintegrate in less than three minutes. The basic approach used in development of MDT is the use of superdisintegrants like sodium starch glycolate which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva.

Thiocolchicoside is a semi-synthetic derivative of the colchicine, a natural anti-inflammatory glycoside which originates from the flower seeds of Superba gloriosa. It is a muscle relaxant with anti-inflammatory and analgesic effects. It has potent convulsant activity and should not administered to individuals prone to seizures.

## EXPERIMENTAL WORK

### Preformulation Study:

Preformulation testing is the first step in rational development of 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.

### Organoleptic Properties:

The drug samples of Thiocolchicoside were studied for appearance, colour and odour.

### Melting Point:

The melting point of the drug substances was determined by using melting point apparatus. The melting point was determined by introducing small amount of substance in the capillary attached to graduated thermometer and constant heat was applied with the assembly suspended in the paraffin bath. The drug sample was tested in temperature range 200-300 $^0$C and point at which drug melts was noted. The melting point is reported in results section.

### Solubility:

To determine solubility of Thiocolchicoside, it was performed in water, Phosphate buffer pH 6.8 and 0.1N HCl. Solubility studies were carried out in glass vials. In each of these vials, 25 ml of each media were added. Excess quantity of drug was added into each of vials. These vials were shaken continuously for 24 hours on a lab shaker and the resulting solutions were filtered, appropriate dilutions were made and UV absorbance were recorded.

### UV spectroscopical analysis:

### Determination of maximum absorbance (λ max)

Stock solutions (100µg/ml) of Thiocolchicoside were prepared in phosphate buffer 6.8. These Solutions were diluted with phosphate buffer 6.8 to obtain suitable conccentrations of each. The UV spectrums were recorded in the range 250-350 nm by using UV-Visible double beam spectrophotometer (Shimadzu 2450). The wavelength of maximum absorption (λ max) was determined.

### Standard Calibration Curve of Thiocolchicoside

10 mg Thiocolchicoside was accurately weighed and transferred to 100 ml volumetric flask. The volume was made up to 100 ml with methanol, 0.1 N HCL, Phosphate Buffer pH 6.8 respectively. Produce stock solution of 100 µg/ml. Working standard solutions of strengths 5,10,15,20,25 µg/ml were made from the stock solution by appropriate dilutions. The above solutions were analyzed by UV spectrophotometer at λ max 259 nm. Methanol, 0.1 N HCL, Phosphate Buffer pH 6.8 respectively was used as blank during spectrophotometric analysis. The standard calibration curve was obtained by plotting absorbance vs. concentration. The concentration range over which the drug obeyed Beer-Lambert's law was chosen as the analytical concentration range.

### Fourier Transform Infrared Spectroscopy of Thiocolchicoside

The infrared spectra of pure Thiocolchicoside were recorded by SHIMADZU 84005 FTIR spectrometer equipped with a Interferometer detector. Samples were prepared by KBr disc method (2 mg sample in 100 mg KBr) and examined in the transmission mode. Each spectrum was measured over a frequency range of 4000–400 $cm^{-1}$

### Drug and Excipient Compatibility:

### FTIR study:

Instrument used was Shimadzu FTIR affinity spectrophotometer. In this study, potassium bromide dispersion method was employed. Pure drug and excipient were analyzed for FTIR studies. The powdered sample was intimately mixed with dry powdered potassium bromide. The mixture was then triturated to powdered dispersion and then placed into analyzer. The dispersion was placed in FTIR spectrophotometer using sample holder and spectrum was recorded.

### Preparation of Powder Blend

Drug Thiocolchicoside and other inactive ingredients except Sodium starch glycolate and Talc were mixed by using glass mortor and pestle and passed through sieve no. 60.The mixed material blended with Sodium starch glycolate and Talc. The whole mixture was passed through Sieve No. 60 twice.

**Table No: Formula For Fast Dissolving Tablet Of Thiocolchicoside**

| Sr. No. | Ingredients(mg) | Formulations | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| 1. | Thiocolchicoside | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| 2. | D-Mannitol | 30 | 30 | 30 | 50 | 50 | 50 | 70 | 70 | 70 |
| 3 | Maltose | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| 4. | Lactose | 60 | 57 | 54 | 40 | 37 | 34 | 20 | 17 | 14 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 5. | Sodium starch glycolate | 2 | 5 | 8 | 2 | 5 | 8 | 2 | 5 | 8 |
| 6. | Saccharine Sodium | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| 7. | Talc | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| 8 | Orange flavour | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. |
| | Total(mg) | 105 | 105 | 105 | 105 | 105 | 105 | 105 | 105 | 105 |

**Evaluations of powder blend:**

**Bulk Density:**

An accurately weighed powder blend from each formula was lightly shaken to break any agglomerates formed and it was introduced in to a measuring cylinder. The volume occupied by the powder was measured which gave bulk volume. bulk density of powder blends was determined using the following formula.

**Bulk density = Total weight of powder / Total volume of powder**

**Tapped density:**

An accurately weighed powder blend from each formula was lightly shaken to break any agglomerates formed and it was introduced into a measuring cylinder. The measuring cylinder was tapped until no further change in volume was noted which gave the tapped volume. The tapped densities (TD) of powder blends were determined using the following formula.

**Tapped bulk density= Total weight of powder / Total volume of tapped powder**

**Angle of repose:**

Angle of repose has been used to characterize the flow properties of solids. It is a characteristic related to inter particulate friction or resistance to movement between particles. The angle of repose (θ) for powder was determined by placing the powder in a funnel. The tip of the orifice of the funnel was fixed from the ground horizontal surface at a height of 1cm and the powder were allowed to flow only under the force of gravity. The angle of repose, θ was calculated from the following relationship.

$$\tan \theta = h/r$$

Where,

**h:** is height of the pile of powder (h=1) and **r** is the radius of the base of cone.

**Table: Standard Values Of Angle Of Repose ($0^0$)**

| Sr. No. | Flow character | Angle of repose($0^0$) |
|---|---|---|
| 1 | Excellent | 25-30 |
| 2 | Good | 31-35 |
| 3 | Fair-aid not needed | 36-40 |
| 4 | passable | 41-45 |
| 5 | Poor | 46-55 |
| 6 | Very poor | 56-65 |
| 7 | Very, very poor | >66 |

**Hausner Ratio:**

Hausner's ratio was determined by following equation,

**Hausner's Ratio=tapped bulk density/Loose bulk density**

A hausner ratio less than 1.12 indicates good flow while greater than 1.35 indicate poor flow.

**Table No.: Standard Values Of Hausener Ratio**

| Sr. No. | Flow Character | Hausner Ratio |
|---|---|---|
| 1 | Excellent | 1.00-1.11 |
| 2 | Good | 1.12-1.18 |
| 3 | Fair-aid not needed | 1.19-1.25 |
| 4 | passable | 1.26-1.34 |
| 5 | Poor | 1.35-1.45 |
| 6 | Very poor | 1.46-1.59 |
| 7 | Very, Very poor | >1.60 |

**Compressibility Index:**

It is a simple index that can be determined on small quantities of powder. In theory, the less compressible a material the more flow able it is. The compressibility indices of the powder blends was determined using following formula,

**Carr's Compressibility Index (%) = [(TBD - LBD)/ TBD] x100**

Relationship between % compressibility and flow ability is shown in the Table No.9

**Table No.: Standard Values Of Carr's Index**

| Sr. No. | Flow Character | Compressibility index (%) |
|---|---|---|
| 1 | Excellent | <10 |
| 2 | Good | 11-15 |
| 3 | Fair-aid not needed | 16-20 |
| 5 | passable | 21-25 |
| 6 | Poor | 26-31 |
| 7 | Very poor | 32-37 |
| 8 | Very, Very poor | >38 |

**Preparation of Mouth Dissolving Tablet**

Tablets were prepared using 6mm round flat-faced punch of the rotary tablet machine [Rimek, Mini Press-1, Karnavti]. Compression force was constant for all formulations. Formula for Mouth Dissolving tablet of Thiocolchicoside is shown in Table No. 6

**Evaluation of MDT of Thiocolchicoside**

**Thickness:**

The thickness of tablet is important for uniformity of tablet size. The thickness of the tablets was determined using a Vernier Calliper. Three tablets from each batch were used.

**Hardness:**

For each formulation, the hardness of three tablets was checked using the Monsanto hardness tester (LAB-HOSP)

**Drug Content Uniformity:**

Five tablets were weighed individually and powdered. The powder equivalent to 10 mg of Thiocolchicoside was weighed and dissolved in water. The volume was made to 100 with water. From this stock solution, 10 µg/ml dilution of the drug was prepared. The drug contents of the resulting solution were calculated from UV absorbance at 259 nm.

**Friability:**

Friability is the measure of tablet strength. In this test number of tablets subjected to combined effect of shock abrasion by utilising a plastic chamber which revolves at a speed of 25rpm, dropping the tablets at a distance of 6 inches in each revolution .A sample of pre-weighed tablets was placed in Roche Friability tester (Kumar Mfg. Ltd.) This was then operated for 100 revolutions. The tablets then dedusted and reweighed. Permitted friability limit is 1.0%. Tablets were then weighed and friability values were determined.

Where,

$$\text{Friability} = \frac{W1 - W2}{W} \times 100$$

W1 = weight of the tablets before test, W2 = weight of the tablets after test

**Weight Variation:**

Twenty tablets were weighed individually. Average weight was calculated from the total weight of all tablets. The individual weights were compared with the average weight. The percentage difference in the weight variation should be within the acceptable limits (±7.5%). The percent deviation was calculated using the following formula.

$$\% \text{ Deviation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

**Table No. 10: Standard Values of Weight Variation**

| Sr. No. | Average weight of tablets (mg) | Maximum percent deviation allowed (%) |
|---|---|---|
| 1 | 80 or less | 10 |
| 2 | Morethan80butlessthan250 | 7.5 |
| 3 | Morethan250 | 5 |

**Wetting Time:**
A piece of tissue paper folded double was placed in a petri dish containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at $37^0$C. Wetting time corresponding to the time taken for the tablet to disintegrate when kept motionless on the tongue was calculated.

**Disintegration Time:**
The *in-vitro* disintegration studies were carried out using Tablet Disintegration Test Apparatus. One tablet was placed in each of the six tubes of the basket assembly and disk was added to each tube. This assembly was then suspended in one-liter beaker containing water maintained at $37\pm2^0$C. The basket was then moved up and down through a distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minutes. The time required for complete disintegration of the tablet was recorded. The test was performed for tablets of all type of formulation (F1-F9)

**Water Absorption Ratio:**
A tablet was placed on the paper and the time required for complete wetting was measur-ed. The wetted tablet was then weighed. Water absorption ratio 'R' was calculated using the equation: R=100 (Wa–Wb)/Wb; where Wa is weight of tablet after water absorption and Wb is weight of tablet before water absorption.

***In- vitro* Drug Release Study:**
An *in-vitro* drug release studies of the prepared nine formulations of Mouth dissolving tablet were conducted for a period of 5 minutes using an eight station USP type 2 apparatus (paddle type) .The agitation speed was 50 rpm. Thiocolchicoside tablet were added to 900 ml of phosphate buffer pH 6.8 at 37 ± 0.5° C. 5 ml aliquots were withdrawn at time intervals of 1,2,3,4 and 5 min. and filtered through Whatmans No. 41 filter paper. An equal volume of fresh dissolution medium was replaced to maintain the volume of dissolution medium. The filtered samples were analysed spectrophotometrically at 259 nm. Cumulative percentage of labelled amount of drug released was calculated.

**Dissolution Kinetics:** [62]
In order to investigate the mode of release from the tablets the release data were analyzed with the following mathematical models:

**Zero –order kinetics:**
The equation for zero order treatment is represented as;

**$Q_o = Q_t + K_o t$**

Where, Qt =amount of drug released in time(t)
Q0=Amount of drug present initially at t=0
K0=zero order release constant

**First-order kinetics:**
The equation for first order treatment is represented as;

**$\log C = \log C_0 - K/2.303$**

Where, C=amount of drug remaining unreleased at time t
C0 =initial amount of drug in solution
K=first order rate constant

**Higuchi's model:**
The simplified Higuchi equation is represented as

**$Q_t = k\, t^{1/2}$**

Where, Qt= amount of drug released in time t

k = Higuchi's constant.

A linear relationship between amount of drug released (Q) versus square root of time ($t^{1/2}$) is observed if the drug release fromthe matrix is diffusion controlled.

**Korsmeyer- Peppas model:**

The Korsmeyer-Peppas model relates drug release exponentially to time. It is described by the following equation;

$Mt/Minf=at^n$

Mt/Minf= fractional release of drug

a= constant depending on structural and geometric characteristics of the drug dosage form

n= release exponent

The value of n indicates the drug release mechanism. For a slab the value n = 0.5 indicates Fickian diffusion and values of n between 0.5 and 1.0 or n = 1.0 indicate non-Fickian mechanism. In case of a cylinder n = 0.45 instead of 0.5, and 0.89 instead of 1.0 .This model is used to analyze the release of drug from polymeric dosage forms, when the release mechanism is not understood or when there is a possibility of more than one type of release mechanisms are involved. Interpretation of diffusional release mechanism from polymeric film are given in (Table: 21)

## RESULTS AND DISCUSSION

### Preformulation Study

### Organoleptic Properties

**Table: Results Of Organoleptic Properties Of Thiocolchicoside**

| Drug | Properties | Observed Result |
|---|---|---|
| Thiocolchicoside | Appearance | Crystalline powder |
| | Colour | Pale Yellow |
| | Odour | Odourless |

All the physical properties of the drugs were within the limit of reported standards which assures the purity of the drug samples.

### Melting Point

**Table: Melting Point Of Thiocolchicoside**

| Drug | Observed | Reported |
|---|---|---|
| Thiocolchicoside | 215-2210C | 2200C |

Melting point of the drugs were within the limit of reported standards which assures the purityof the drug samples.

### 1o.1.3 Solubility Study of Thiocolchicoside

**Table No. 15: Solubility Profile Of Thiocolchicoside**

| Sr.no. | Solvent | Solubility(µg/ml) |
|---|---|---|
| 1 | Water | 8.30 |
| 2 | PhosphatebufferpH6.8 | 4.65 |
| 3 | 0.1NHCl | 5.634 |

Solubility of the drug was found to be in water 8.30µg/ml, in phosphate buffer 6.8 4.65 µg/ml and in 0.1 N HCL 5.634 µg/ml which assures the purity of the drug samples.

**Ultraviolet Spectroscopy**

**Determination of absorbance maximum (λ max )**

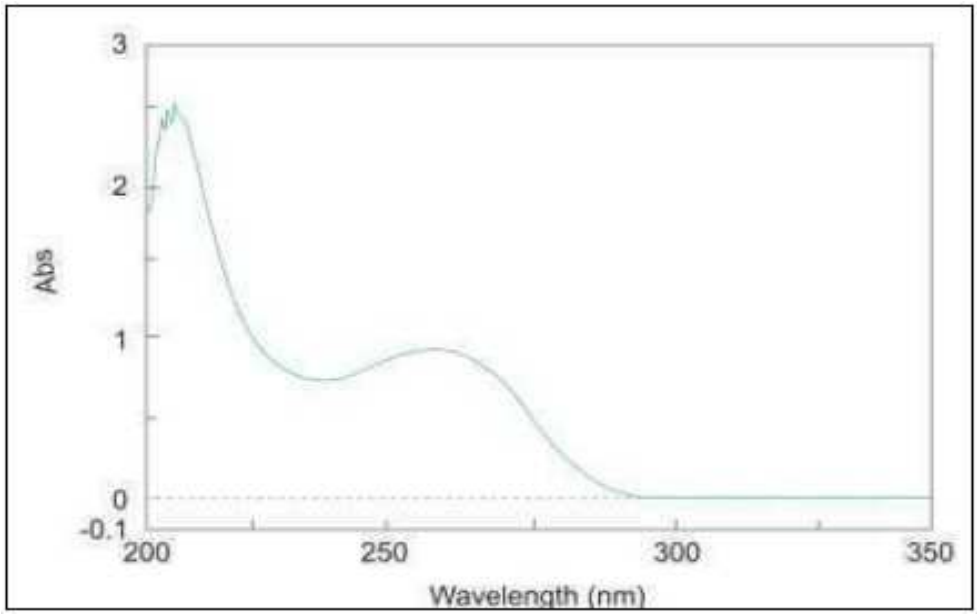


**Fig..: λ max of Thiocolchicoside in Phosphate buffer 6.8**

**Table No. 13: λ MAX of Thiocolchicoside in phosphate buffer 6.8**

| Name of drug | λmax(nm) |
|---|---|
| Thiocolchicoside | 259 |

Wavelength of maximum absorption was found to be 259 nm for Thiocolchicoside in Phosphate buffer 6.8. The drug content of formulation was determined at the same wavelength in Phosphate buffer 6.8.

**Calibration Curve of Thiocolchicoside in methanol**

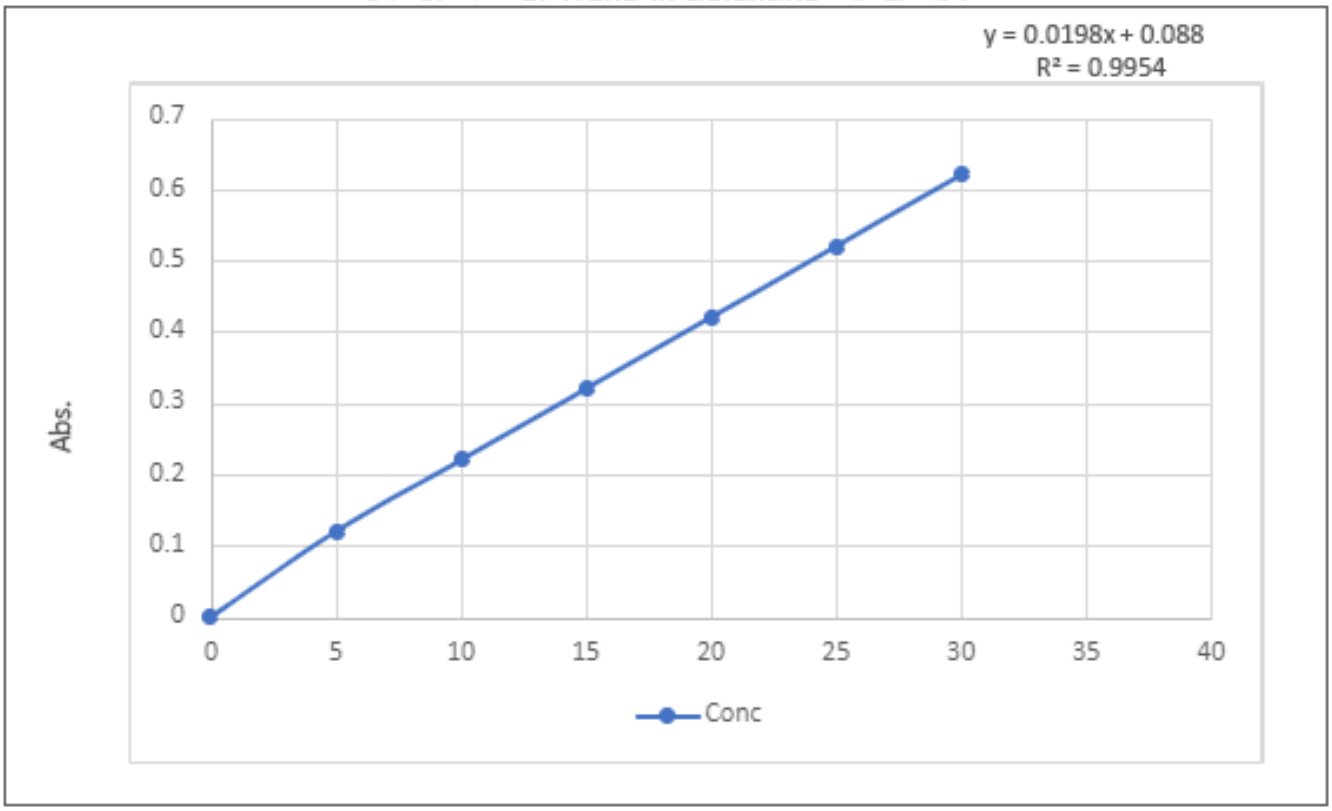


**Fig.: Calibration Curve of Thiocolchicoside in Methanol**

Methanolic solution of drug was very clear and readily analyzed by UV spectrophotometer. The data of absorbance vs. concentration were plotted on graph and the values of $R^2$ were determined. A linear relationship was obtained in between concentration (5-25 µg/ml) and absorbance of Thiocolchicoside in Methanol with $R^2$ value of 0.995 at 259 nm show in .fig.

**Calibration Curve of Thiocolchicoside in 0.1 N HCl**

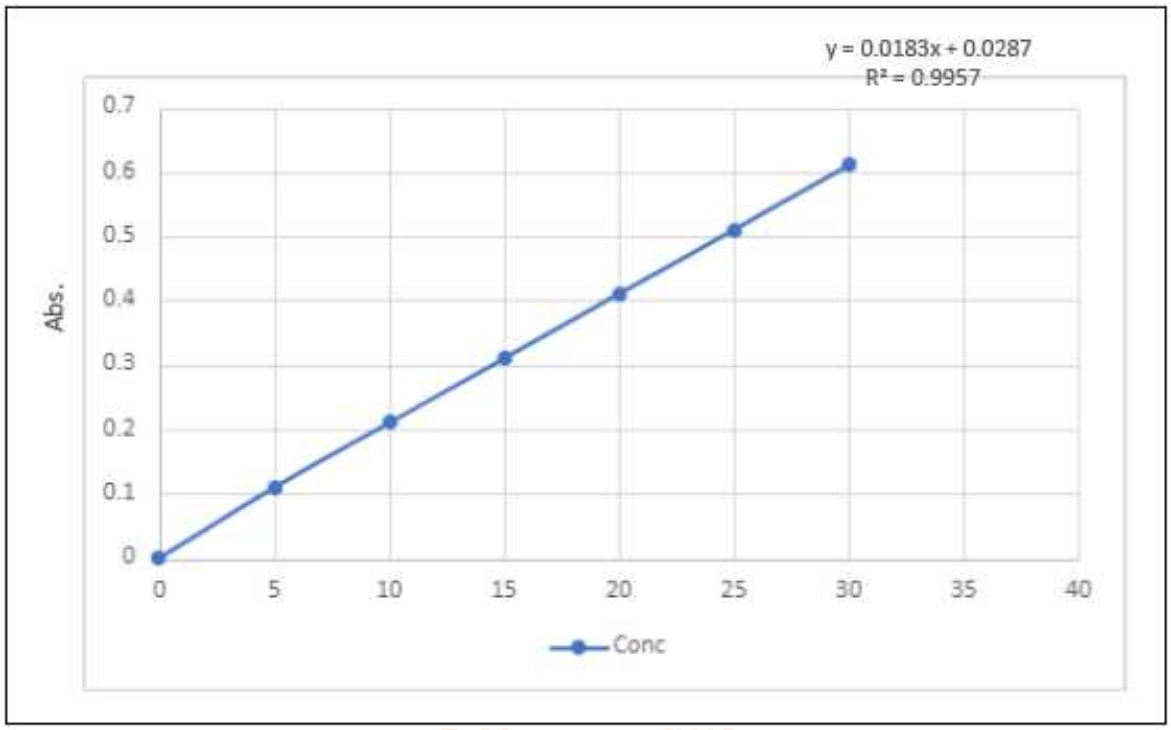


**Fig.: Calibration Curve of Thiocolchicoside in 0.1N HCl**

Calibration curve of Thiocolchicoside was performed in 0.1 N HCl since dissolution studies were carried out in these media. A linear relationships was obtained in between concentration (5-25 µg/ml) and absorbance of Thiocolchicoside in 0.1 N HClwith R2 value of 0.9957 at 259 nm is shown in Fig.

**Calibration Curve of Thiocolchicoside in Phosphate buffer pH 6.8**

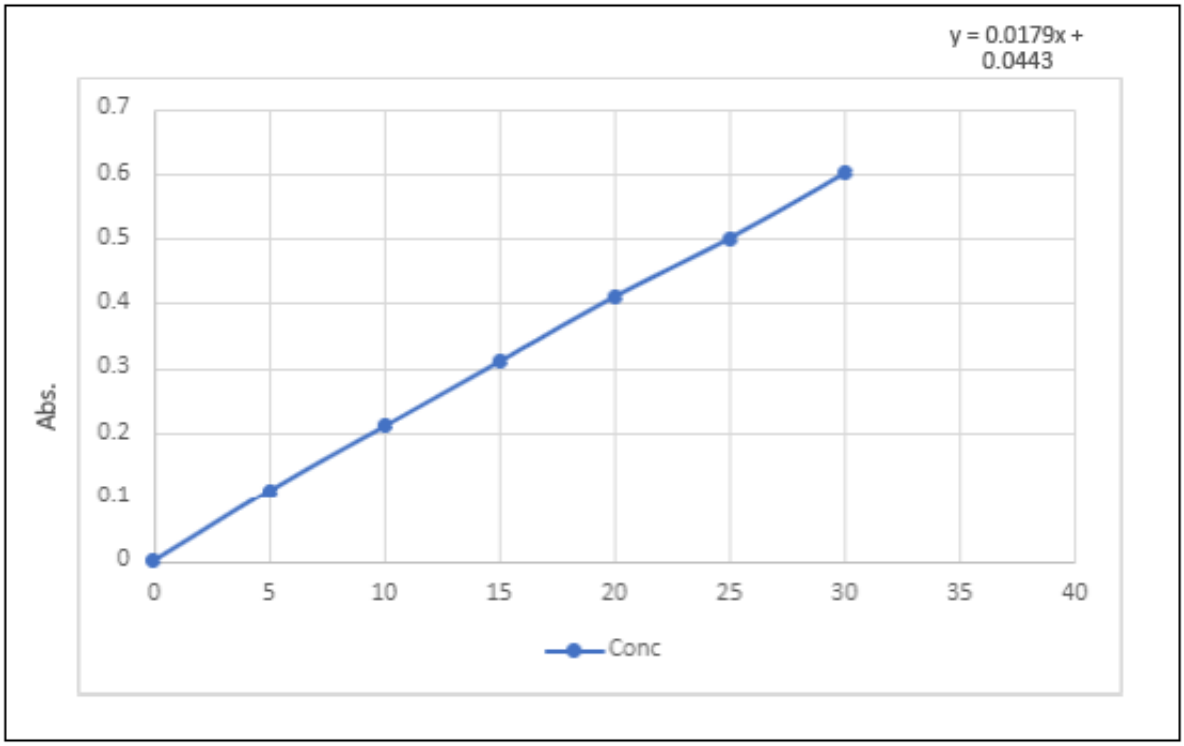


**Fig.: Calibration Curve of Thiocolchicoside in Phosphate buffer pH 6.8**

Calibration curve of Thiocolchicoside was performed in phosphate buffer pH 6.8 since dissolution studies were carried out in these media. A linear relationship was obtained in between concentration (5-25µg/ml) and absorbance of Thiocolchicoside in Phosphate buffer pH 6.8 with $R^2$ value of 0.9909 at 259 nm is shown in Fig.

**Fourier Transform Infrared (FT- IR) study of Thiocolchicoside**

FT-IR study of Thiocolchicoside was carried out to check the purity of drug. FTIR spectrum of Thiocolchicoside is shown in Fig.No.12 and the interpretations of IR frequencies are shown in Table No.

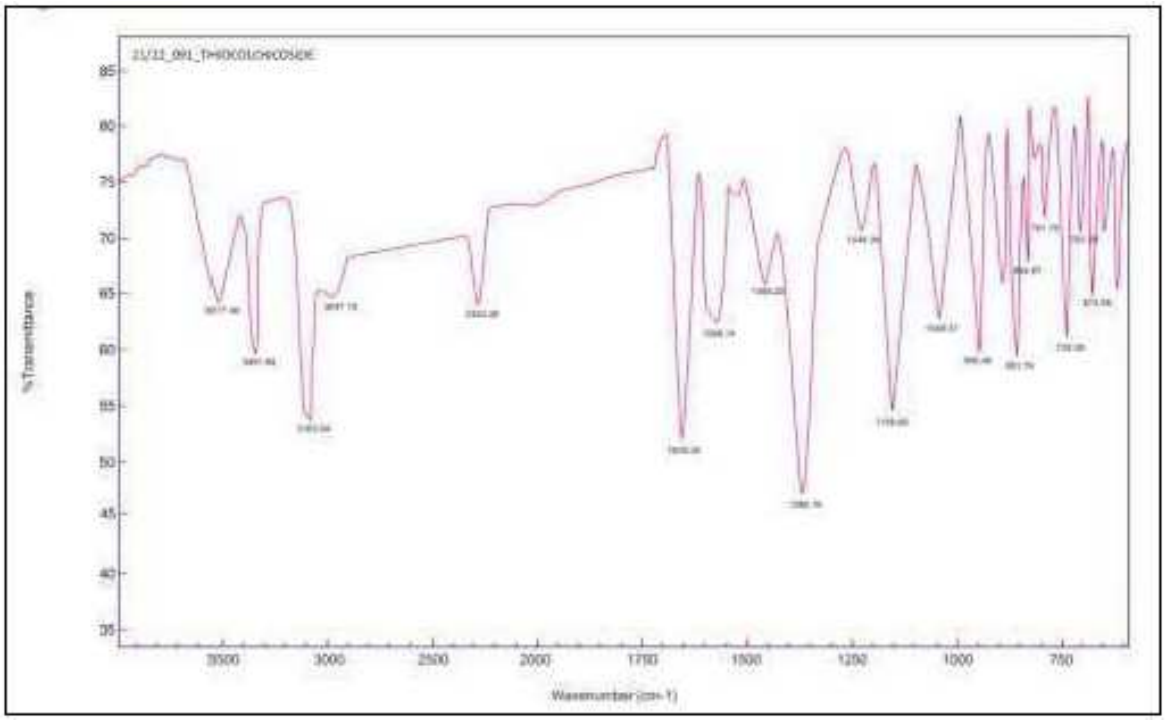

**Fig. No.: FT-IR Spectrum of Thiocolchicoside**

**Table No. 16: FTIR Peaks of Thiocolchicoside**

| Observed Values Peaks (cm-1) | Standard Values Peaks (cm-1) | Spectrum of Thiocolchicoside Assignment |
|---|---|---|
| 3163.54 | 3220-3100 | NH- stretching |
| 2343.26 | 2350-2300 | CH-stretching |
| 1679.45 | 1700-1600 | C=Ostretching |
| 1386.76 | 1400-1350 | -COO stretching vibration |
| 1139.68 | 1150-1100 | C-C stretch |
| 851.79 | 900-830 | C-H rocking |

Major functional groups present in Thiocolchicoside show characteristic peaks in IR spectrum. Table No.16 shows peaks observed at different wave numbers and the functional group associated with these peaks. The major peaks were identical to functional group of Thiocolchicoside. Hence, the purityof sample was confirmed.

**Drug and Excipient Compatibility Study**

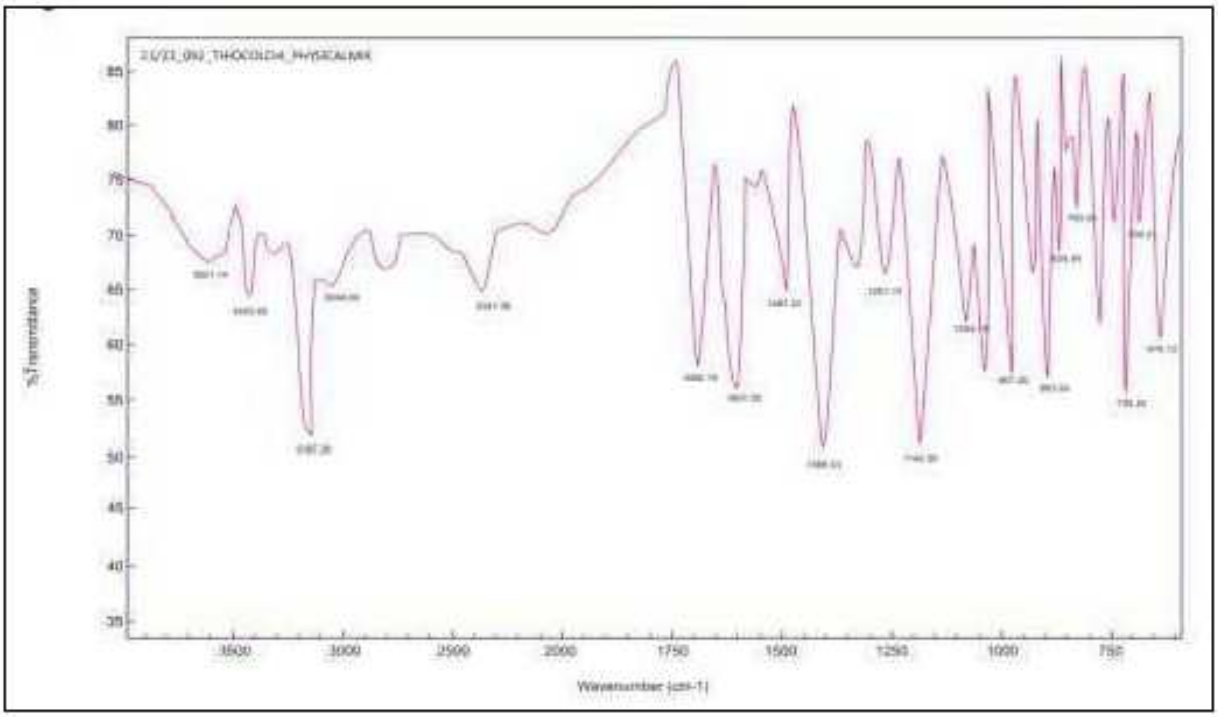

**Fig. No.: FT-IR study of Physical Mixture**

| Observed Values Peaks (cm-1) | Standard Values Peaks (cm-1) | Spectrum of Thiocolchicoside Assignment |
|---|---|---|
| 1740-1720 | 1742.49 | C=Ostretching |
| 3220-3100 | 3162.52 | N-H-stretching |
| 1385-1380 | 1380.76 | -COO stretching vibration |
| 1150-1100 | 1142.67 | C-C stretch |

The presence of absorption bands corresponding to the functional groups N-H Stretching amines. The absence of any well-defined unaccountable peaks is a confirmation of the purity of the drug sample. From above spectrum, it was found that Thiocolchicoside is compatible mixture of all excipient.

**Preparation of powder blend:**
The powder blends was prepared by mixing of various ingredients.

Mentioned inTable No.6

**Evaluation of powder blend:**

| formulation batches | Physica lproperties* | | | | |
|---|---|---|---|---|---|
| | Bulk density (gm/ml) | Tapped density (gm/ml) | Angle of repose (0C) | Compressibility Index (%) | Hausner Ratio |
| F1 | 0.4321±0.015 | 0.505±0.04 | 28.79±0.60 | 14.00±1.14 | 1.16±0.017 |
| F2 | 0.4734±0.002 | 0.518±0.02 | 26.57±1.37 | 7.90±0.48 | 1.08±0.05 |
| F3 | 0.4645±0.004 | 0.525±0.05 | 25.97±1.97 | 12.03±1.59 | 1.13±0.017 |
| F4 | 0.5544±0.004 | 0.522±0.03 | 27.14±0.61 | 12.76±0.78 | 1.14±0.01 |
| F5 | 0.4764±0.013 | 0.551±0.05 | 26.34±0.66 | 8.19±1.89 | 1.08±0.02 |
| F6 | 0.4535±0.007 | 0.529±0.02 | 28.34±1.14 | 14.01±0.46 | 1.15±0.01 |
| F7 | 0.4483±0.003 | 0.523±0.06 | 27.03±0.99 | 14.44±0.77 | 1.16±0.01 |
| F8 | 0.4639±0.016 | 0520±0.05 | 29.48±1.19 | 11.85±2.09 | 1.13±0.02 |
| F9 | 0.4685±0.006 | 0.524±0.03 | 28.26±1.05 | 11.5±1.84 | 1.12±0.02 |

**Table: Evaluation Of Powder Blend**

**Bulk Density:**
The powder blends of formulations have the bulk density ranged between 0.4321 to 0.5544 gm/ml.

**Tapped density:**
The powder blends of formulations have the tapped bulk density ranged between 0.505 to 0.551 gm/ml.

**Angle of repose:**
The flow properties of blend were analyzed by determining angle of repose which was found to be between 25-30 indicating excellent flow property.

**Hausner's Ratio:**
The hausner ratio for the formulations was found to be <1.00-1.11, indicating excellent flow properties and 1.12-1.18 indicating good flow property

**Carr's Compressibility Index:**
The carr's index for the formulations was found to be below <10% indicating that the powders have a excellent compressibility and 11-15 indicating good compressibility

**Formulation Mouth dissolving tablet by direct compression method**
The present work undertaken to formulate and evaluated Mouth dissolving tablet of Thiocolchicoside by direct compression method. Superdisintegrant at different concentration were included to assist Mouth disintegration.

**Evaluation of tablets:**
All batches of prepared tablets were evaluated for the different parameters.

**Table No.: Evaluation Of Thiocolchicoside Mouth Dissolving Tablets**

| Formulation batches | Parameters | | | |
|---|---|---|---|---|
| | Thickness (mm) (±SD) | Hardness (Kg/cm2) (±SD) | Drug content (%) (± SD) | Friability (%) (± SD) |
| F1 | 2.82±0.04 | 2.43±0.05 | 96.04±0.99 | 0.54±0.02 |
| F2 | 2.88±0.08 | 2.50±0.07 | 99.60±0.90 | 0.72±0.11 |
| F3 | 2.68±0.04 | 2.83±0.08 | 98.55±1.91 | 0.71±0.12 |
| F4 | 2.78±0.08 | 2.56±0.50 | 97.21±0.66 | 0.64±0.12 |
| F5 | 2.73±0.07 | 2.40±0.50 | 96.04±0.91 | 0.68±0.05 |
| F6 | 2.84±0.15 | 2.40±0.28 | 97.99±1.19 | 0.70±0.01 |
| F7 | 2.65±0.07 | 3.40±0.28 | 97.04±1.10 | 0.73±0.03 |
| F8 | 2.69±0.20 | 3.1±0.28 | 96.42±0.68 | 0.28±0.01 |
| F9 | 2.72±0.88 | 2.83±0.57 | 97.99±1.90 | 0.70±0.02 |

| Formulation batches | Parameters | | | |
|---|---|---|---|---|
| | Weight variation (mg)(±SD) | Wetting time (sec.) (± SD) | Water absorption ratio (%) (± SD) | Disintegration Time (sec.) (± SD) |
| F1 | 105.26±1.10 | 15.7±1.48 | 76.48±1.68 | 46.±0.83 |
| F2 | 104.83±1.02 | 11.0±0.83 | 54.39±0.76 | 33 ±0.81 |
| F3 | 105.24±1.06 | 17.2±3.38 | 68.43±1.68 | 52±1.26 |
| F4 | 105.56±1.27 | 25.6±2.77 | 78.48±1.31 | 56.33±1.36 |
| F5 | 105.56±1.04 | 31.2±2.34 | 69.33±2.51 | 51.83±1.72 |
| F6 | 105.32±1.67 | 41.2±2.38 | 69.52±1.76 | 40.21±1.94 |
| F7 | 105.86±1.55 | 36.6±2.30 | 64.18±1.53 | 43.5±2.07 |
| F8 | 105.49±1.70 | 42.2±4.76 | 68.18±0.70 | 45 ±2.44 |
| F9 | 105.00±0.80 | 36.00±1.87 | 58.15±1.66 | 52 ±1.97 |

**Thickness:z**

Thickness of Tablet formulations was found to be ranging from 2.65 mm to 2.88 mm. Variation of thickness in Tablet formulations (F1 to F9) was found within the acceptable limits.

**Hardness:**

Hardness of Tablet formulations was found to be ranging from 2.40 Kg/cm$^2$ to 3.40 Kg/cm$^2$. Results obtained are within acceptable limit.

**Drug content uniformity study:**

Percent drug content of Thiocolchicoside was found in between 96.04%.-99.60%

**Friability:**

Friability of Tablet formulations was found to be ranging from 0.28% to 0.73% which is within the acceptable limits.

**Weight variation:**

Weight variation of tablet formulation was found to be in 104.83 mg to 105.56 mg which is within acceptable limit.

**Wetting time:**

Wetting time of all formulation (F1-F9) was found in between the 11 to 42 sec.

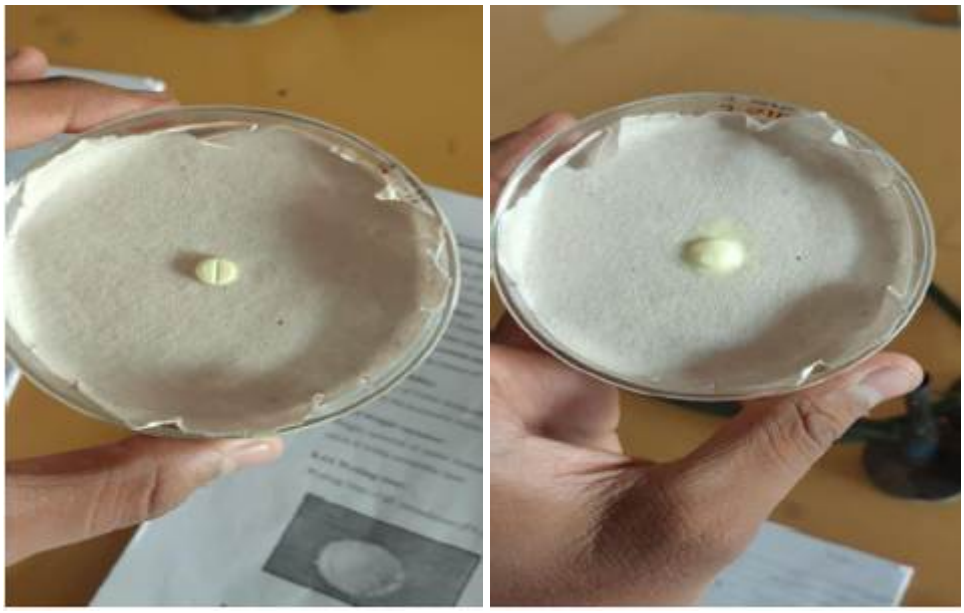

**Fig. No. 15: Tablet Before - After Wetting**

**Water absorption ratio**

The water absorption ratio was found to be in between the 54% to78%.

**Disintegration time**

Mouth dissolving Tablets should disintegrate within three minute. Three Tablets of each formulation were taken and placed in 6 tubes of disintegration apparatus. The time taken for complete disintegration was noted. The disintegration time for formulation F1-F9 was found to be in the range of 33 to 56 sec.

***In-vitro* drug Release Study of Thiocolchicoside MDT**

**Dissolution Data of Mouth Dissolving Tablets of Thiocolchicoside**

| Formulation Code % CDR | Time | | | | |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 |
| F1 | 43.64±3.54 | 65.71±0.90 | 72.67±1.80 | 89.46±1.40 | 94.44±0.39 |
| F2 | 45.26±1.67 | 69.37±1.36 | 82.96±1.51 | 91.65±1.16 | 96.83±0.03 |
| F3 | 32.17±2.29 | 53.26±0.56 | 77.97±1.82 | 85.11±1.22 | 94.56±1.01 |
| F4 | 35.39±2.53 | 45.16±1.77 | 60.17±2.62 | 78.88±1.33 | 93.56±1.01 |
| F5 | 40.55±2.74 | 53.42±2.49 | 65.06±1.23 | 83.77±2.95 | 94.27±1.82 |
| F6 | 39.43±0.50 | 58.65±2.02 | 73.65±2.10 | 85.12±3.43 | 94.97±0.77 |
| F7 | 35.22±2.78 | 54.43±2.41 | 74.16±3.58 | 83.77±1.91 | 92.76±1.27 |
| F8 | 44.48±1.77 | 59.63±1.38 | 75.00±1.17 | 83.27±0.77 | 95.92±0.58 |
| F9 | 34.03±1.77 | 53.25±2.04 | 71.63±0.77 | 84.45±2.62 | 92.21±0.76 |

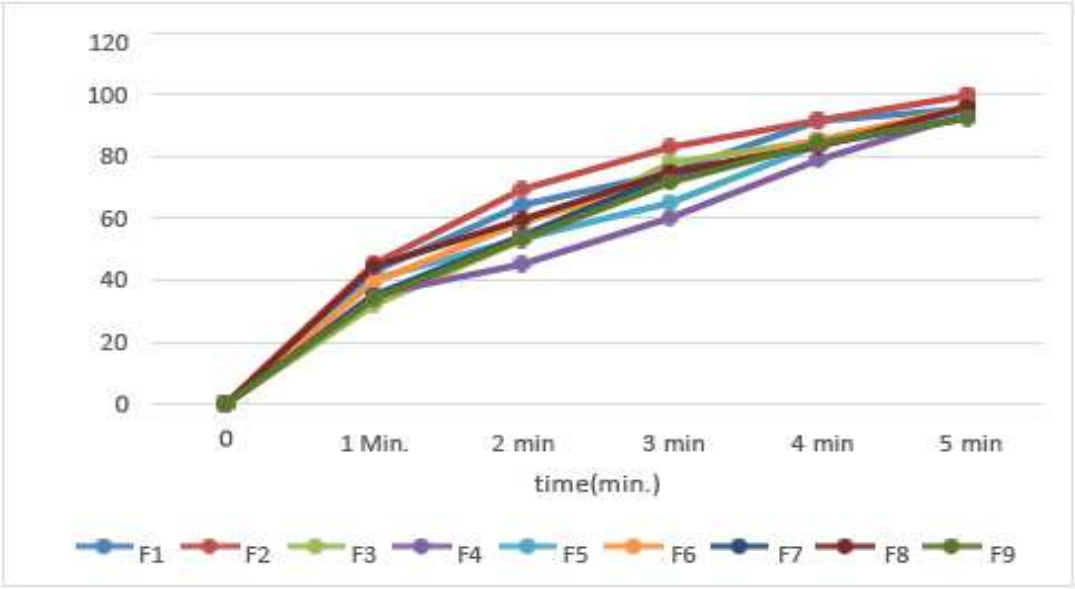


**Fig. No. 16: Dissolution profile of Mouth Dissolving Tablets of Thiocolchicoside**

Percent drug release data expressed in Table 19 and Fig.16 Indicate In-Vitro release study was shown 96.83% release of Thiocolchicoside through F2 formulation in 5 minutes. Formulation F2 showed less disintegration time and percent cumulative drug release 96.83% so it was declared as an optimized formulation and was subjected for further evaluation and stability studies.

**Table No. 20: Evaluation Parameters of F2 Optimized Batch**

| Sr. No. | Parameters | Results* |
|---|---|---|
| 1 | Weight variation (mg) | 104.83±1.10 |
| 2 | Thickness (mm) | 2.88±0.08 |
| 3 | Hardness (kg/cm2) | 2.50±0.07 |
| 4 | Friability (%) | 0.72±0.11 |
| 5 | Wetting time (sec) | 11.00±0.83 |
| 6 | Disintegration time (sec) | 33.00±0.81 |
| 7 | Uniformity of content (%) | 96.83±0.90 |
| 8 | Water absorption ratio (%) | 54.39±0.76 |

**Table No.: Results of In-Vitro Dissolution Study of Optimized Batch**

| Sr. No. | Time(min) | % Cumulative drug release* |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 1 | 45.26±1.67 |
| 3 | 2 | 69.37 ±1 |
| 4 | 3 | 82.96±1.80 |
| 5 | 4 | 91.65±1.16 |
| 6 | 5 | 96.83±0.03 |

(* mean of three values ± SD)

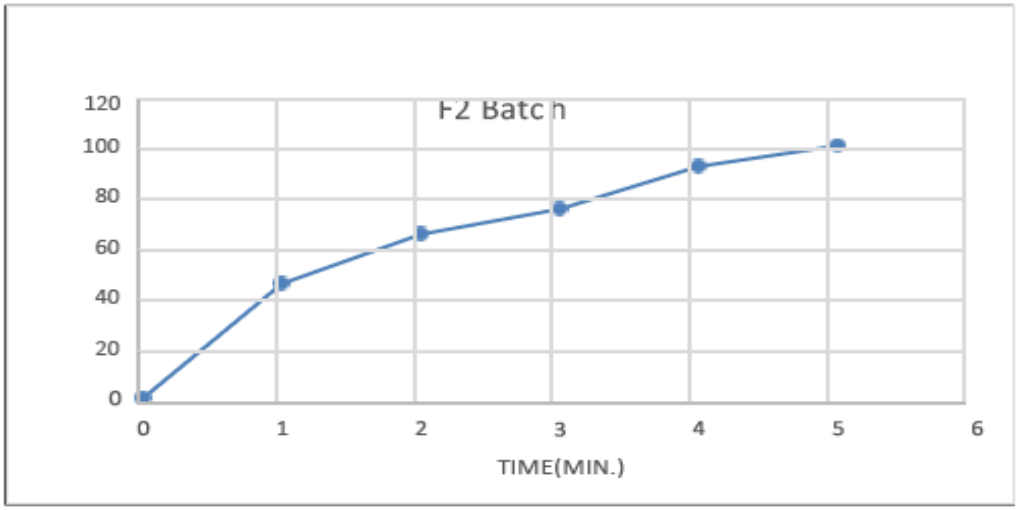


**Fig. No. 17: Graphical presentation of dissolution profile of optimized batch**

**Dissolution kinetic study of Mouth Dissolving Tablets**

To analyze the mechanism of drug release from the tablet, data obtained from the drug release studies was subjected to different mathematical models (Zero order, First order, Matrix (Higuchi) and Korsemeyer's Peppas). The correlation coefficient ($r^2$) was used as an indicator for the best fitting for each of the models. Table no.22,23,24 and Table No.25. shows the Kinetics treatment for the optimized formulations. Different mathematical models for drug release mechanism of Mouth Dissolving Tablets were shown in the Figure No. 18,19,20 and 21 respectively.

**Zero order comparative evaluation model kinetics:**

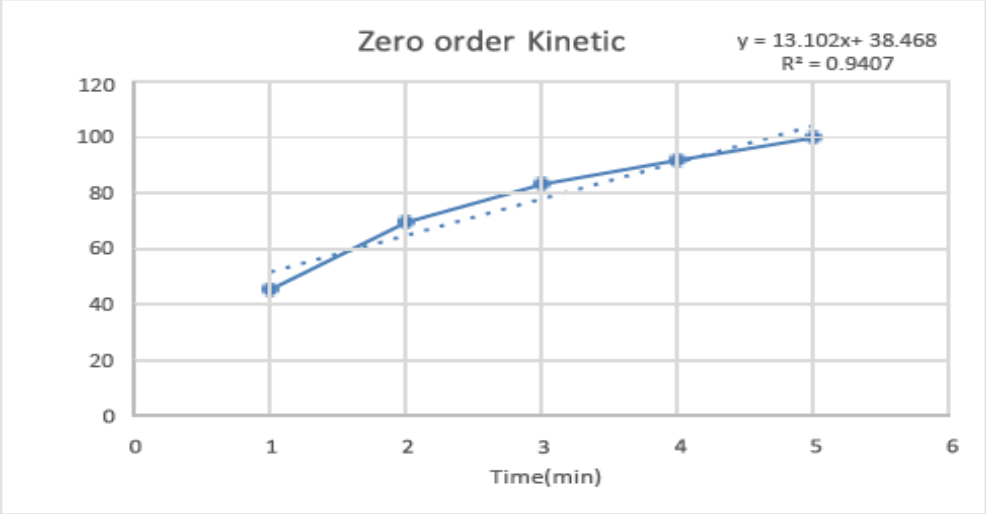


**Figure No. 18: Model graph for comparative evaluation of Zero order releasekinetics**

**Table No.: $R^2$ values for first order release kinetics**

| Batch | F2 |
|---|---|
| R2 value | 0.9407 |

**First order comparative evaluation model kinetics:**

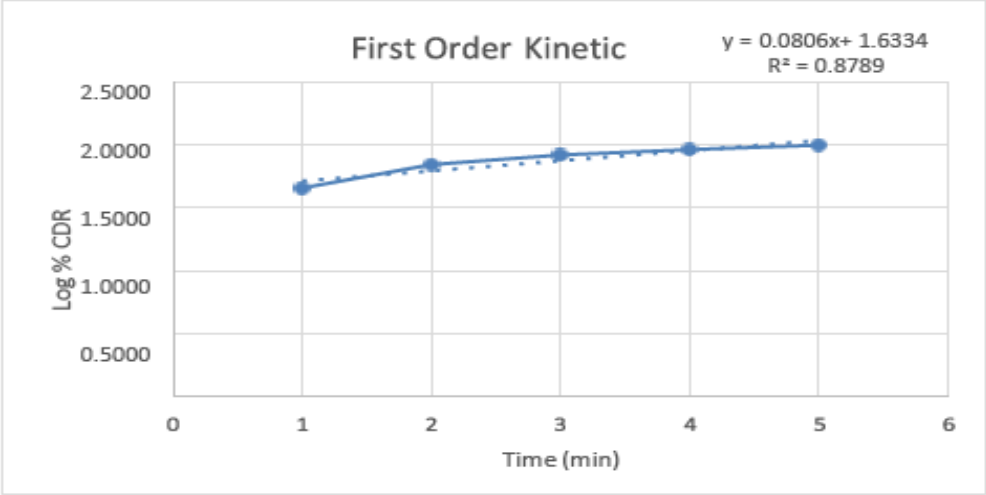


**Figure No. 19: Model graph for comparative evaluation of first order releasekinetics**

**Table No.: $R^2$ values for first order release kinetics**

| Batch | F2 |
|---|---|
| R2 value | 0.8789 |

**Higuchi and Connor's model release kinetics:**

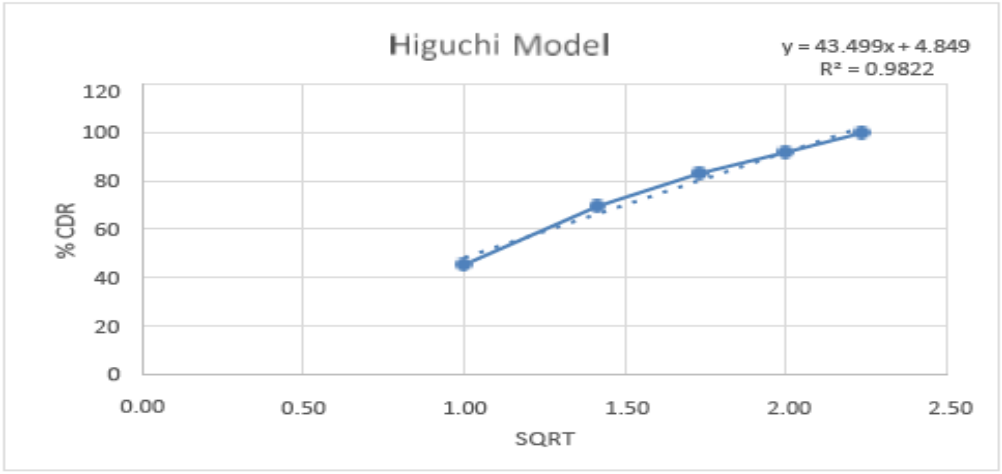


**Figure No.: Model graph for comparative evaluation of Higuchi and Connor's release kinetics.**

**Table No.: $R^2$ values for Higuchi and Connor's release kinetics**

| Batch | F2 |
|---|---|
| R2 value | 0.9822 |

**Korsemeyer's peppas of release kinetics:**

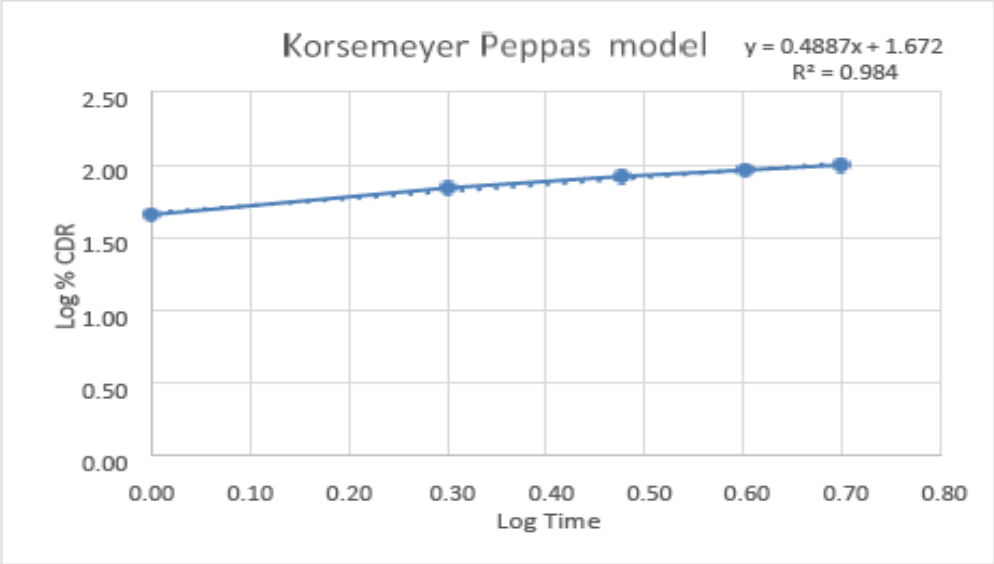


**Figure No.: Model graph for comparative evaluation Korsemeyer's peppas of release kinetics.**

**Table No. 25: R2and n values for Korsemeyer's peppas release kinetics**

| Batch | F2 |
|---|---|
| R2 value | 0.984 |

**Discussion:** From the $R^2$ value it was concluded that the drug release profile of Thiocolchicoside Mouth Dissolving Tablets followed korsemeyer's-peppas release pattern. The classical zero order release curve was found to be linear ($r^2 = \geq 0.9407$). The curves plotted according to Higuchi release model were also found to be linear. ($r^2 = \geq 0.982$ for Higuchi model data) respectively. For the korsemeyer's-peppas release curve $R^2$ values of all batches was found to be $\geq 0.984$ and 'n' value was found to be $\geq 0.586$ which indicates that all the formulations show anomalous (non- fickian release). The drug release occurs probably by dissolution.

## SUMMARY AND CONCLUSIONS

The present study was aimed to formulate and evaluate the Mouth dissolving tablet of Thiocolchicoside. Preliminary investigation of drug was carried out with different parameters;

### 1. Melting Point:-217°C

Compatibility of drug with polymers was confirmed by FT- IR study. Tablet were prepared with super disintegrants like Sodium starch glycolate, and other ingredients such as Mannitol, Lactose, Maltose, Sodium saccharide and Talc by Direct compression technique. It was observed that the results obtained after evaluation of (F2) formulations follows standards prescribed for Mouth dissolving tablets. The tablet were evaluated for various evaluation parameters such as, Weight Variation, Thickness, Hardness, Friability, wetting time, water absorption ratio, I*n-vitro* Disintegration Time, *in-Vitro* drug release study, and uniformity of Content etc. Mouth dissolving tablet of optimized formulation (F2) having Mouth disintegration, better dissolution and all necessary parameter within the range. Formulation F2 shows the highest drug release upto 96.63%. Finally it is concluded that the drug release from the Mouth dissolving tablet was increased by using the increased concentration of superdisintegrant upto certain conc. After increase in conc. Of superdisintegrant leads to decrease disintegration in the buccal cavity. Increased systemic availability of drug will lead to quick onset of action, which is a prerequisite for analgesic activity.

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