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# FORMULATION AND EVALUATION OF ACECLOFENAC MATRIX TABLETS BY USING NATURAL POLYMERS

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**Keywords:**

Aceclofenac, sustained release, guar gum, matrix tablets, gum tragacanth, Natural polymers

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## ABSTRACT

In recent year sustained release dosage forms continue to draw attention in the search for improved patient compliance and decreased incidence of adverse drug reactions. Sustained release technology is relatively cow field and as a consequence, research in the field has been extremely fertile and has produced many discoveries. Aceclofenac is an NSAID (non-steroidal anti inflamatory drug). Formulation of matrix tablets of the drug may prolong the therapeutic concentration of drug in blood and will improve the efficacy and patient compliance and also the dosing frequency can be reduced. Usage of natural polymers will improve the sustained release of drug and the cost can be reduced ultimately. Hence, an attempt was made to formulate matrix tablet of Aceclofenac drug using natural polymers. FTIR spectroscopy was performed to find out the possible interaction between the drug Aceclofenac and the polymers Guar gum and Tragacanth gum. Aceclofenac matrix tablets were formulated by wet granulation method. The polymer concentration was studied by using different polymer ratios. The granules were evaluated for bulk density, tapped density, angle of repose and carr's index. The values of carr's index and angle of repose signify good flowability of the granules for all the batches. The tablets were evaluated for hardness, weight variation, thickness, content uniformity and friability which comply with the standards. The *in vitro* release of the drug Aceclofenac form the prepared tablets is studied by using 6.8 phosphate buffers for 24 hours. The polymers guar gum and tragacanth gum had sustained the release of drug from the tablets. From all the prepared formulations, the ideal formulation was selected based on physicochemical properties and *in vitro* release studies. The ideal formulations G-3 and T-2 were subjected to release kinetics. The drug release from the tablets was zero order diffusion controlled and release mechanism was Fickian.

## INTRODUCTION

Oral route has been the commonly adopted and most convenient route for the drug delivery .oral route of administration has been received more attention in the pharmaceutical field, because of the more flexibility in the designing of dosage form than drug delivery design for other routes. The oral drug delivery depends on various factors such as type of delivery system, the disease being treated, the patient, the length of the therapy and the properties of the drug most of the oral controlled drug delivery systems relay on diffusion, dissolution, or combination of both mechanisms, to release the drug in a controlled manner to the gastro intestinal tract. The physicochemical properties include crystal nature, solubility, partition coefficient, intrinsic dissolution etc. dosage form characteristics are controlled and optimized with respect to the physicochemical properties of the drug and relevant gastro intestinal environmental factors. Other factors need to be considered are diseased state, the patient compliance & length of therapy. The goal of targeted oral drug delivery systems is to achieve better therapeutic success compared to conventional dosage form of the same drug[1]. Successful fabrication of sustained release products is usually difficult & and involves consideration of physicochemical properties of drug, pharmacokinetic behavior of drug, route of administration, disease state to be treated and, most importantly, placement of the drug in dosage form total will provide the desired temporal and spatial delivery pattern for the drug

The slow first order release obtained by a sustained release pre parathion is generally achieved by the release of the drug from a dosage form. In some cases, this achieved by making slow the release of drug from a dosage form and in other cases, this is accomplished by a continuous release process[2].

Guar gum is a galactomannan, commonly used in cosmetics, food products, and pharmaceutical formulation. Guar gum linear chains of (1→4)-β-D-mannopyranosyl units with α-D-galactopyranosyl units attached by (1→6) linkages. The ratio of D-galatose to D-mannose is between 1:1.4 and 1:2. It has also been investigated in the preparation of sustained-release matrix tablets in the place of cellulose derivatives such as methylcellulose[3]. Saleh M. Al-Saidan *et al* developed guar gum matrix tablets for oral controlled release of water-soluble diltiazem hydrochloride[4]. Varshosaz *et al* developed a sustained release matrix tablet for highly water soluble tramadol hydrochloride using natural gums (xanthan and guar gum) as cost effective, nontoxic, easily available, and suitable hydrophilic matrix systems compared with the extensively investigated hydrophilic matrices (ie, HPMC/carboxymethyl cellulose with respect to *in vitro* drug release rate) and hydration rate of the polymers. Matrix tablets of tramadol were produced by direct compression method[5].

Tragacanth is a naturally occurring dried gum obtained from Astragalus gummifer Labillardie`re and other species of Astragalus grown in Western Asia. The gum consists of a mixture of water-insoluble and watersoluble polysaccharides. Bassorin, which constitutes 60–70% of the gum, is the main water-insoluble portion, while the remainder of the gum consists of the water-soluble material tragacanthin[6]. Dhruba Sankar Goswami *et al* using various hydrophilic polymers such as HPMC, Sodium alginate, Tragacanth, Sodium CMC and hydrophobic polymer EC prepared mucoadhesive tablets to reduce dosing frequency[7]. MD Sajid Ali *et al* developed sustained release matrix tablets of phenytoin sodium by the wet granulation method using water as granulating agent along with matrix materials like guar gum, sodium alginate, tragacanth and xanthan gum with varying percentage[8].

## MATERIALS AND METHODS

Aceclofenac has been taken as the model drug and PVP K30 has been used as a binding agent, lactose has been used as a diluent, fumaric acid is used as an acidulant. Magensium stearate and talc has been used as lubricant and glidant respectively. Methyl paraben sodium is used as a preservative. All the samples were from KNISS labarotories Pvt. Ltd, Chennai.

### Drug-Excipient Compatibility Studies

Infrared (IR) spectroscopy was conducted using a FTIR Spectrophotometer and the spectrum was recorded. The procedure consisted of dispersing a sample (drug alone or mixture of drug and excipients) in KBr and compressed into discs by applying a pressure of 5 tons for 5 min in a hydraulic press. The pellet was placed in the light path and the spectrum was obtained.

### Preparation of Matrix Tablets

The tablets were prepared by wet granulation technique. The compositions of the tablet formulations are given in Table 6.5. Weighed amounts of aceclofenac, polymer gum (guar gum/tragacanth), and diluents (lactose), Preservative (sodium propyl paraben) and stabilizer (fumaric acid) were taken into a bowl by passing through a 40 mesh screen and mixed manually for 5 min. Then the blend was granulated with PVPK-30 using water as the granulating agent. The mass was dried in tray drier at 50°C and sieved through a 30 mesh screen. Magnesium stearate, talc and colloidal silicon dioxide were then added to the dried, sieved granules and mixed for about 5 min in a poly-bag. The produced mixture was compressed into tablets using a 16 station tablet compression machine, (Cadmach). The batch was coated using the coating solution and using a laboratory coater under controlled condition. The efficiency of mixing was verified by the determination of drug content[9].

**Characterization of Aceclofenac compressed tablets**

**Pre compression parameters**

**i. Bulk density (Db)**

The bulk density of the formulated granules was evaluated using a bulk density apparatus. It is the ratio of to total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder into a graduated measuring cylinder and the volume was noted. It is expressed in gm/ml and is given by

$$Db = \frac{M}{Vb}$$

Where, M - Mass of the powder

Vb – Bulk volume of the powder

**ii. Tapped density (Dt)**

It is the ratio of total mass of powder to the tapped volume of powder. The tapped volume was measured by tapping the powder to constant volume. It is expressed in gram/ml and is given by

$$Dt = \frac{M}{Vt}$$

Where, M - Mass of the powder

Vt – Tapped volume of the powder.

**iii. Carr's index (I)**

Carr's index is a measure the propensity of granule to be compressed and the flow ability of granule. Carr's index was calculated using following formula.

$$I = \frac{Dt - Db}{Dt} \times 100$$

Where, Dt – Tapped density of the powder

Db – Bulk density of the powder[10].

**iv. Angle of repose**

The frictional forces in a loose powder can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powder and the horizontal plane. Sufficient quantities of granules were passed through a funnel from a particular height (2 cm) onto a flat surface until it formed a heap, which touched the tip of the funnel. The height and radius of the heap were measured. The angle of repose was calculated using the formula

Angle of repose $\mathbf{\theta = \tan^{-1}(h/r)}$

Where, h – Height of the pile in cm

r – Radius of the pile.

**Post compression parameters**

**I. Hardness**

The prepared tablets were subjected to hardness test. It was carried out by using hardness tester and expressed in $kg/cm^2$.

**II. Friability (F)**

The friability was determined using Roche friabilator and expressed in percentage (%). 20 tablets from each batch were weighed separately ($W_{initial}$) and placed in the friabilator, which was then operated for 100 revolutions at 25 rpm. The tablets were reweighed ($W_{final}$) and the percentage friability was calculated for each batch by using the following formula.

$$F = \frac{(W_{initial}) - (W_{final}) \times 100}{(W_{initial})}$$

**III. Weight variation test**

20 tablets were selected at random from the lot, weighed individually and the average weight was determined. The percent deviation of each tablets weight against the average weight was calculated. The test requirements are met, if not more than two of the individual weights deviate from the average weight by not more than existing 7.5%[11].

**IV. Content uniformity**

An accurately weighed amount of each preparation was dissolved in small volume of methanol and further diluted with methanol. The content of aceclofenac was determined spectrophotometrically at 275 nm using Shimadzu UV-visible spectrophotometer.

**V. *In-vitro* Release Rate Studies**

The *in vitro* dissolution study was carried out using USP Type 2 dissolution apparatus. The study was carried out in 900 ml of phosphate buffer pH 6.8 from 2 to 24 h. The dissolution medium was kept in a thermostatically controlled water bath, maintained at 37 ± 0.5°C. The paddle was lowered so that the lower end of the stirrer was 25 mm above the base of the beaker. The pre-weighed tablet was then introduced into the dissolution jar and the paddle was rotated at 50 rpm. At different time intervals, 10 ml sample was withdrawn and analyzed spectrophotometrically at 275 nm for drug release. At each time of withdrawal, 5 ml of fresh corresponding medium was replaced into the dissolution flask[12].

**RELEASE KINETICS**

Data obtained from the *in vitro* release studies were fitted to various kinetic equations such as zero order, first order, Higuchi model, Hixson Crowell Cube root law and Korsmeyer- Peppas model.

**Zero order equation**

$Q = Q_0 - K_{0t}$

**First order equation**

$In\ Q = In\ Q_0 - K_{1t}$

**Higuchi equation**

$Q = K^2t^{1/2}$

**Korsmeyer - Peppas equation**

$Q/Q_0 = K_{tn}$

Where, $K_0$ to $K_2$ were release rate constants, Q/Q0 was fraction of drug released at time t, K was a constant and n was diffusion constant that indicates general operating release mechanism. For Fickian (diffusion controlled), $n \leq 0.5$; for non- Fickian (anomalous) release, 'n' value is in between 0.5 to 1.0; for zero order release, n=1.0, for super case transport II, n > 1.040.

**Hixson-Crowell Cube Root Equation**

The Hixson-Crowell cube root law describes the release from systems where there is a change in surface area and diameter of particles or tablets.

$$Q_0^{1/3} - Q_t^{1/3} = KHC\ t$$

Where, Qt is the amount of drug released in time t, Q0 is the initial amount of the drug in tablet and KHC is the rate constant for Hixson-Crowell rate equation. The following plots were made cumulative % drug release vs. time (zero order kinetic model), log cumulative of % drug remaining vs. time (first order kinetic model), cumulative % drug release vs. square root of time (higuchi model), log cumulative % drug release vs. log time (korsmeyer model) and cube root of drug % remaining in matrix vs. time (hixsoncrowell cube root law)[13].

**Mechanism of drug release**

Korsmeyer *et al* derived a simple relationship which described drug release from a polymeric system .To find out the mechanism of drug release, first 60% drug release data was fitted in Korsmeyer–Peppas model,

$$Mt / M\infty = Kt\, n$$

Where, $Mt / M\infty$ is the fraction of drug released at time t, k is the rate constant and n is the release exponent. The n value is used to characterize different release mechanisms as given in the following table for cylindrical shaped matrices. Diffusion exponent and solute release mechanism for cylindrical shape[14].

**Table: 1 Diffusion exponent '*n*' and mechanism of diffusional release from CDDS**

| Sno. | Slab | Cylinder | Sphere | Drug release mechanism |
|---|---|---|---|---|
| 1 | 0.5 | 0.45 | 0.43 | Fickian diffusion |
| 2 | >0.5-<1.0 | >0.45-<0.89 | >0.43-<0.85 | Anamalous transport (non-Fickian) |
| 3 | 1.0 | 0.89 | 0.85 | Zero-order release |
| 4 | >1.0 | >0.89 | >0.85 | Case-II transport |
| 5 | >>1.0 | >1.0 | >1.0 | Super case-II transport |

**RESULTS**

**FT-Infrared spectroscopy to find out the compatibility of drug with polymers**

An FT infrared (FT-IR) spectroscopy study was carried out to check the compatibility between the drug aceclofenac and the polymers guar gum and tragacanth gum used for the preparation of aceclofenac release matrix tablets. The FT-IR was performed for drug, polymers, and physical mixture of drug and polymers. The spectra obtained from FT infrared spectroscopy studies at wavelength from 2000 $cm^{-1}$ to 400 $cm^{-1}$.

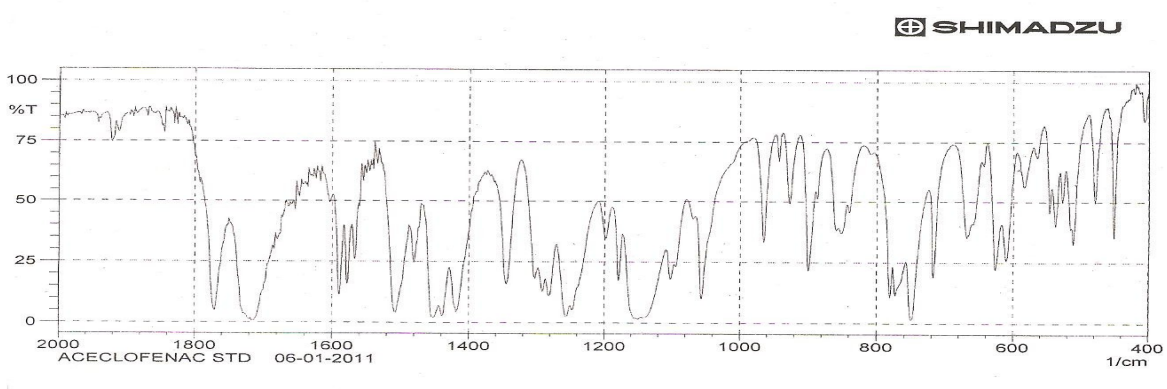


**Fig: 1 IR Spectrum of Pure Aceclofenac drug**

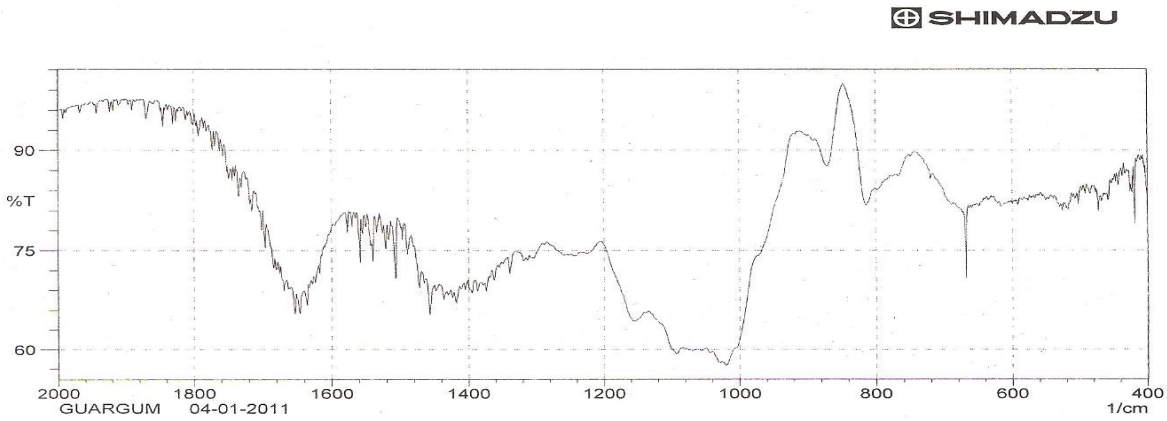


**Fig: 2 IR Spectrum of Polymer Guar Gum**

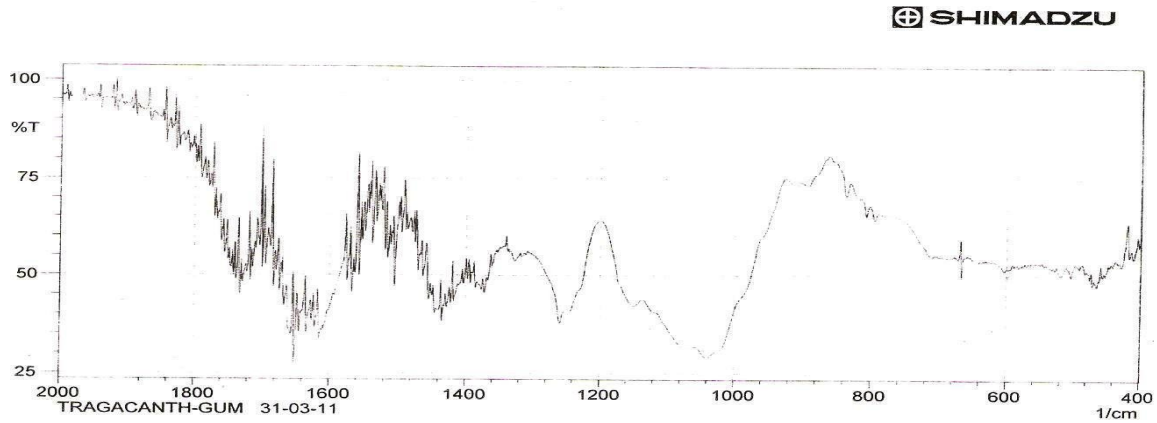


**Fig: 3 IR Spectrum of Polymer Tragacanth Gum**

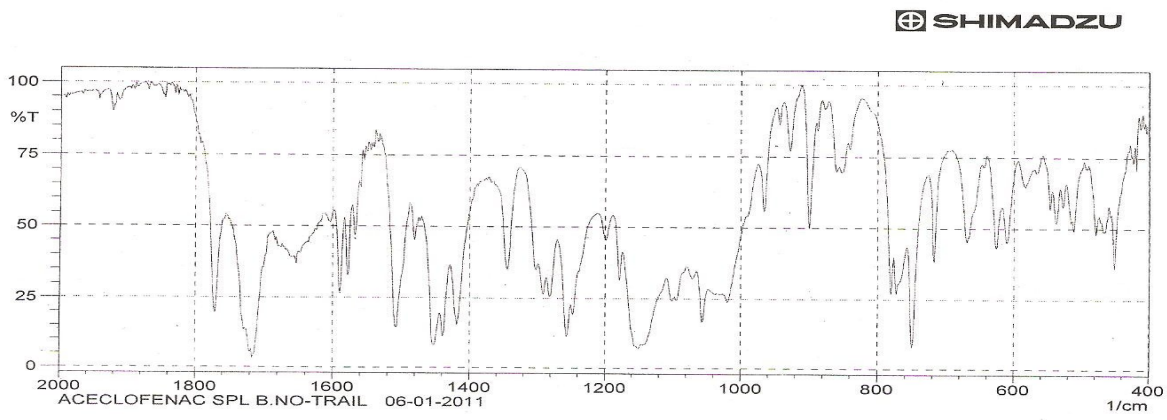


**Fig: 4 IR Spectrum of Aceclofenac + Guar gum (Trial G-3)**

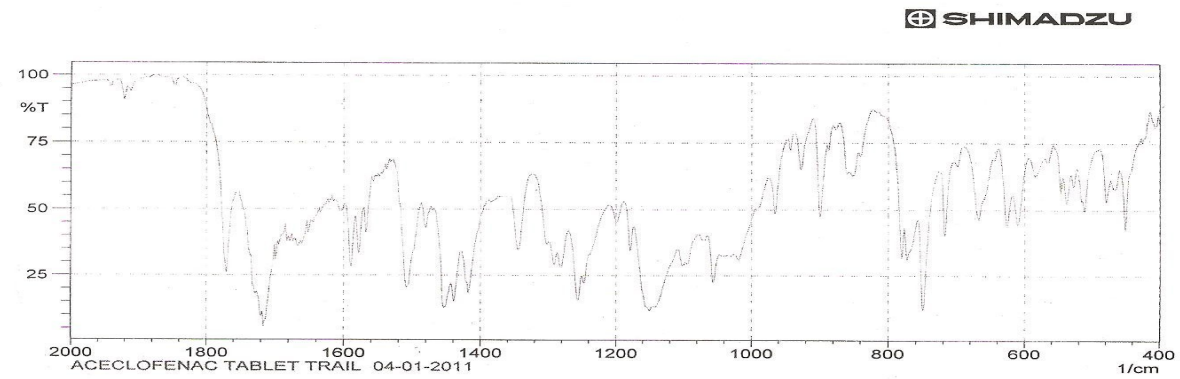


**Fig: 5 IR Spectrum of Aceclofenac + Tragacanth gum (Trial T-2)**

**Table: 2 IR studies of drug and mixture of drug-polymer**

| SNO. | SAMPLE | DIFFERENT PEAKS | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Pure aceclofenac | 1775 | 1713 | 1591 | 1578 | 1569 | 1500 | 1480 | 1458 | 1439 | 1417 |
| 2 | Aceclofenac + Guar gum | 1769 | 1718 | 1592 | 1574 | 1568 | 1497 | 1477 | 1457 | 1440 | 1419 |
| 3 | Aceclofenac + Tragacanth gum | 1764 | 1719 | 1590 | 1577 | 1561 | 1504 | 1483 | 1455 | 1440 | 1421 |

| SNO. | SAMPLE | DIFFERENT PEAKS | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Pure aceclofenac | 1339 | 1308 | 1289 | 1282 | 1256 | 1243 | 1199 | 1176 | 1112 | 1058 |
| 2 | Aceclofenac + Guar gum | 1333 | 1301 | 1294 | 1283 | 1253 | 1242 | 1198 | 1180 | 1115 | 1058 |
| 3 | Aceclofenac + Tragacanth gum | 1336 | 1314 | 1289 | 1285 | 1257 | 1249 | 1199 | 1173 | 1177 | 1060 |

The IR studies were carried out for pure Aceclofenac, Acelcofenac + guar gum and Aceclofenac + Tragacanth gum tablets by using KBr pellet method, to check the compatibility between drug and carriers. The IR spectras are shown in figures 7.1(a), 7.1(b), 7.1(c), 7.1(d), 7.1(e). The principle peaks of Aceclofenac pure drug were found at different wavenumbers as mentioned in tables which corresponds to the theoretical peaks at different wavenumbers as mentioned in tables 7.1. From these interpretations it is evident that there is no interaction between drug and polymers.

**Standard Curve of Aceclofenac**

A standard solution containing 1 mg/ ml of aceclofenac was prepared in methanol by dissolving 25 mg of pure aceclofenac in 50 ml of methanol. From this solution, working standard solutions of concentrations 0 to 20 µg/ml of aceclofenac was prepared by dilution with methanol. The absorbance of the solutions was measured at 276 nm against reagent blank.

**Table: 3 Standard curve of Acelcofenac**

| SNO. | CONCENTRATION (mcg/ml) | ABSORBANCE |
|---|---|---|
| 1 | 4 | 0.116 |
| 2 | 8 | 0.221 |
| 3 | 12 | 0.328 |
| 4 | 16 | 0.429 |
| 5 | 20 | 0.526 |

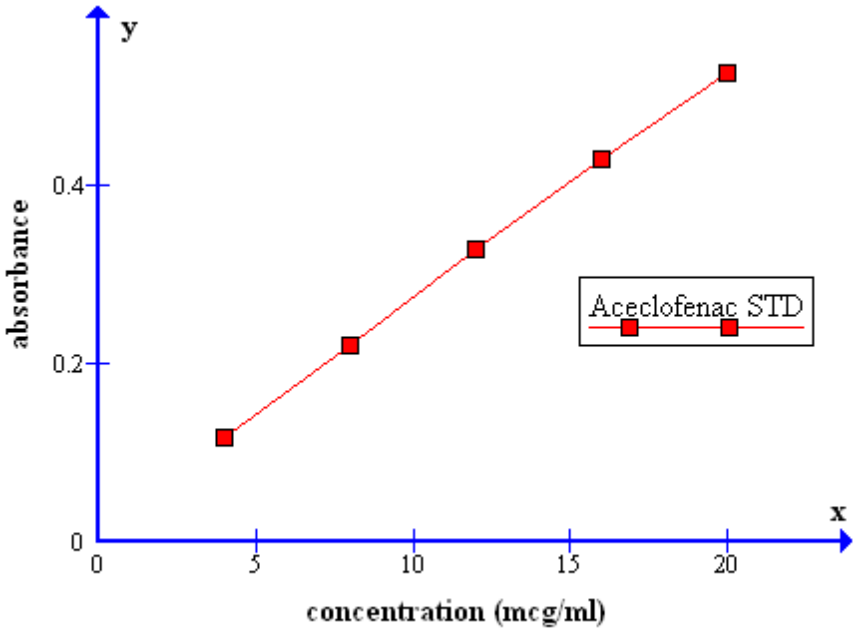


**Fig: 6 Standard curve of Aceclofenac**

**Characterization of Aceclofenac tablets**

**Pre compression parameters**

The granules were prepared by wet granulation method. The granules were evaluated for angle of repose, bulk density, tapped density and compressibility index, and the results are shown in Table. The bulk densities of the granules were found to be in the range of 0.43 to 0.51 gm/ml. The angle of repose varied from 16°43' to 21°25'. The tapped densities were ranged 0.48 to 0.62 gm/ml, the carr's indexes were in the range of 10.5 to 22.6.

**Table: 4 Physicochemical evaluations of Aceclofenac granules**

| SNO. | FORMULATIONS | ANGLE OF REPOSE (°) | BULK DENSITY (g/ml) | TAPPED DENSITY (g/ml) | CARR'S INDEX (%) |
|---|---|---|---|---|---|
| 1 | G-1 | 20.4±0.88 | 0.48±0.01 | 0.62±0.03 | 22.6±1.66 |
| 2 | G-2 | 16.43±0.65 | 0.43±0.01 | 0.48±0.03 | 10.5±0.87 |
| 3 | G-3 | 19.62±0.69 | 0.44±0.06 | 0.51±0.01 | 13.8±0.35 |
| 4 | T-1 | 21.25±0.87 | 0.51±0.01 | 0.59±0.02 | 13.6±0.45 |
| 5 | T-2 | 20.55±0.59 | 0.47±0.02 | 0.55±0.04 | 14.6±0.7 |

**Post compression parameters**

The Aceclofenac tablets were prepared by wet granulation method. The results of physicochemical evaluation of prepared tablets are shown in. The tablets were evaluated for weight variation, drug content, hardness and friability. The drug content was found to be between 98.55% to 107.13%. The hardness was found to be from 1 to 8 (kg/cm2) and in all the cases the friability was less than 1%.

**Table: 5 Physicochemical evaluations of Aceclofenac tablets**

| SNO. | FORMULATIONS | THICKNESS (mm) | WEIGHT VARIATION (%) | HARDNESS ($Kg/cm^2$) | DRUG CONTENT (%) | FRIABILITY (%) |
|---|---|---|---|---|---|---|
| 1 | G-1 | 4.55±0.02 | 1.21±0.04 | 7±0.5 | 98.55±0.03 | 0.02±0.04 |
| 2 | G-2 | 4.32±0.03 | 2.13±0.02 | 5±1 | 99.21±0.07 | 0.03±0.01 |
| 3 | G-3 | 4.52±0.05 | 2.54±0.03 | 8±1 | 107.13±0.12 | 0.07±0.01 |
| 4 | T-1 | 4.74±0.03 | 3.04±0.02 | 6±2 | 99.4±0.08 | 0.04±0.01 |
| 5 | T-2 | 4.38±0.02 | 2.15±0.04 | 7±1 | 99.56±0.97 | 0.03±0.01 |

**Fig: 7 Aceclofenac Tablets (G-3)**

**Fig: 8 Side view of the tablet (G-3)**

**Fig: 9 Aceclofenac Tablets (T-2)**

**Fig: 10 Side view of the tablet (T-2)**

**Table: 6 Data of *in vitro* drug release studies**

| SNO. | TIME (hours) | ACECLOFENAC+ GUAR GUM (%) | | | ACECLOFENAC+TRAGACANTH (%) | |
|---|---|---|---|---|---|---|
| | | TRIAL 1 | TRIAL 2 | TRIAL 3 | TRIAL 1 | TRIAL 2 |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 2 | 41.42±1.41 | 34.31±2.04 | 25.55±1.13 | 32.46±1.15 | 20.07±0.55 |
| 3 | 4 | 67.43±1.48 | 57.16±1.31 | 34.31±1.62 | 52.14±1.2 | 25.49±0.39 |
| 4 | 6 | 98.79±0.54 | 78.13±1.24 | 44.31±1.25 | 79.14±1.5 | 32.16±0.87 |
| 5 | 8 | - | 98.14±0.94 | 52.01±3.14 | 99.81±0.75 | 39.28±1.09 |
| 6 | 12 | - | - | 60.31±0.74 | - | 50.56±1.34 |
| 7 | 24 | - | - | 98.27±1.29 | - | 98.97±0.47 |

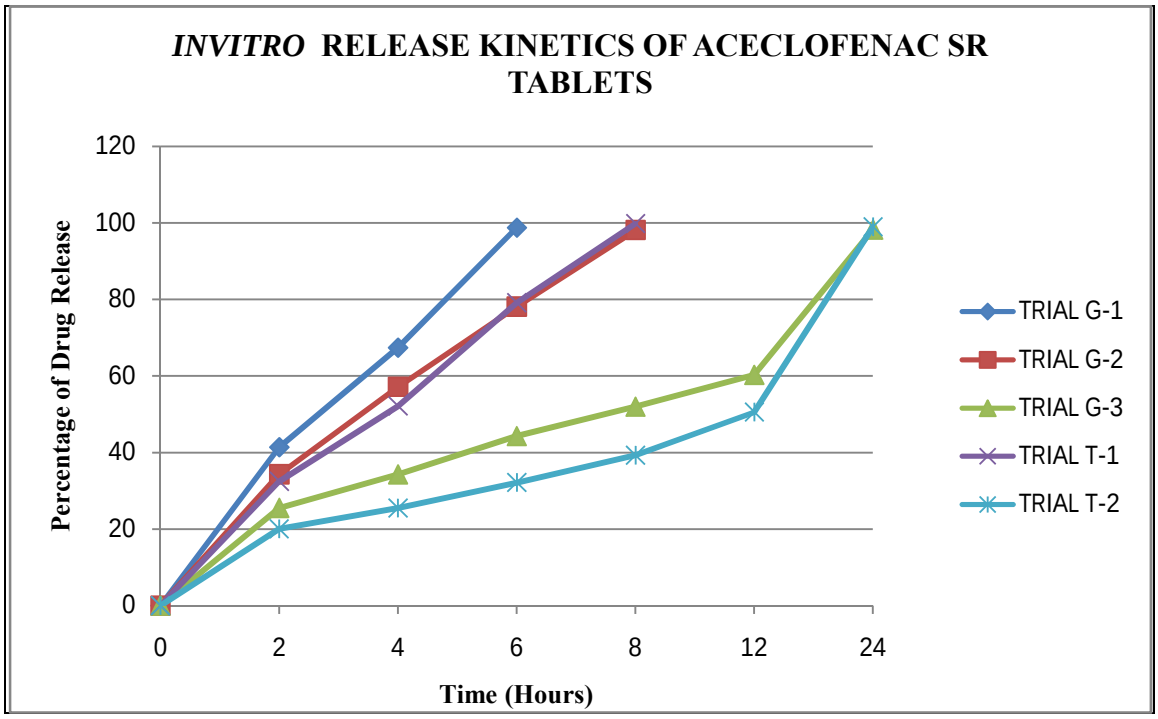


**Fig 11 Data of *in vitro* drug release studies**

**RELEASE KINETICS OF ACECLOFENAC TABLET FORMULATIONS**

**ZERO ORDER RELEASE KINETICS**

**Table: 7 Zero Order Release Kinetics**

| SNO. | FORMULATION | CUMULATIVE % DRUG RELEASE | | | | | |
|---|---|---|---|---|---|---|---|
| | | TIME (hours) | | | | | |
| | | 2 | 4 | 6 | 8 | 12 | 24 |
| 1 | G-1 | 41.42% | 68.03% | 99.94% | - | - | - |
| 2 | G-2 | 34.31% | 57.67% | 79.07% | 99.63% | - | - |
| 3 | G-3 | 25.55% | 34.64% | 44.89% | 52.93% | 61.51% | 100.01% |
| 4 | T-1 | 32.46% | 52.61% | 80.1% | 101.27% | - | - |
| 5 | T-2 | 20.08% | 25.75% | 32.61% | 39.92% | 51.73% | 100.45% |

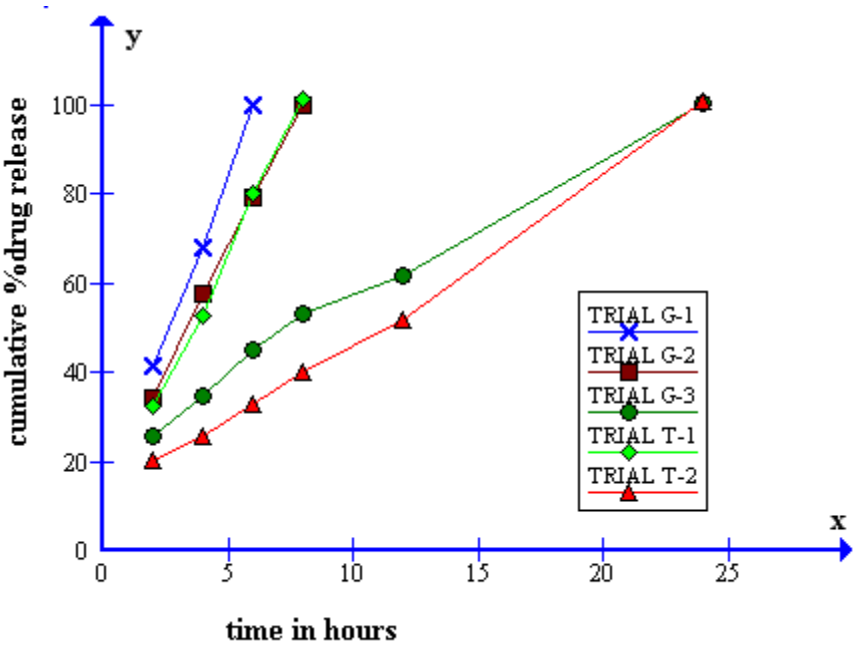


**Fig: 12 Zero order release kinetics of formulations G-1,G-2,G-3,T-1,T-2**

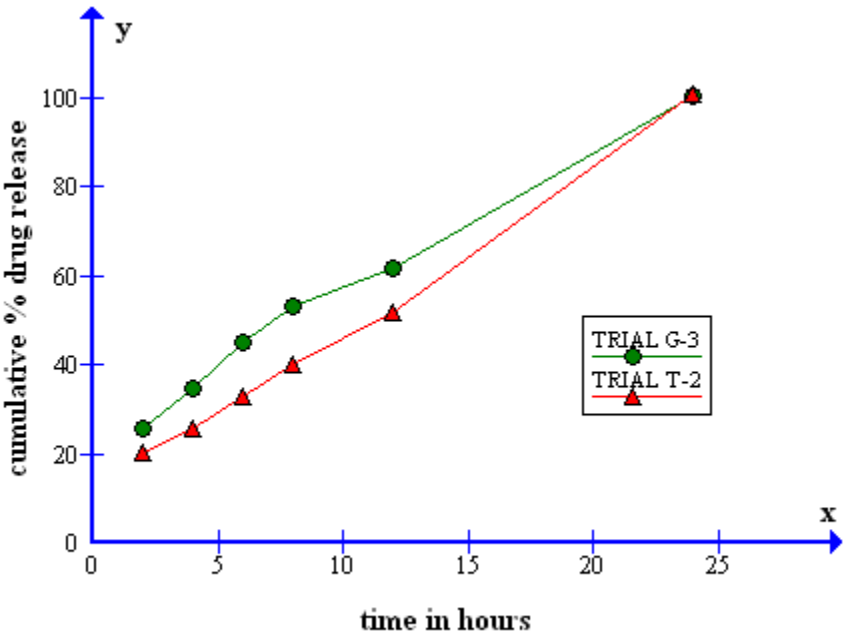


**Fig: 13 Zero order release kinetics of formulations G-3,T-2**

**HIGUCHI MODEL RELEASE KINETICS**

**Table: 8 Higuchi Model Release Kinetics**

| SNO. | SQUARE ROOT OF TIME IN (hours) | CUMULATIVE % DRUG RELEASE | | | | |
|---|---|---|---|---|---|---|
| | | TRIALG- 1 | TRIAL G-2 | TRIALG- 3 | TRIAL T-1 | TRIAL T-2 |
| 1 | 2 | 41.42% | 34.31% | 25.55% | 32.46% | 20.07% |
| 2 | 4 | 68.09% | 57.67% | 34.64% | 52.61% | 25.75% |
| 3 | 6 | 99.94% | 79.07% | 44.89% | 80.1% | 32.61% |
| 4 | 8 | - | 99.63% | 52.93% | 101.27% | 39.92% |
| 5 | 12 | - | - | 61.51% | - | 51.73% |
| 6 | 24 | - | - | 100.01% | - | 100.45% |

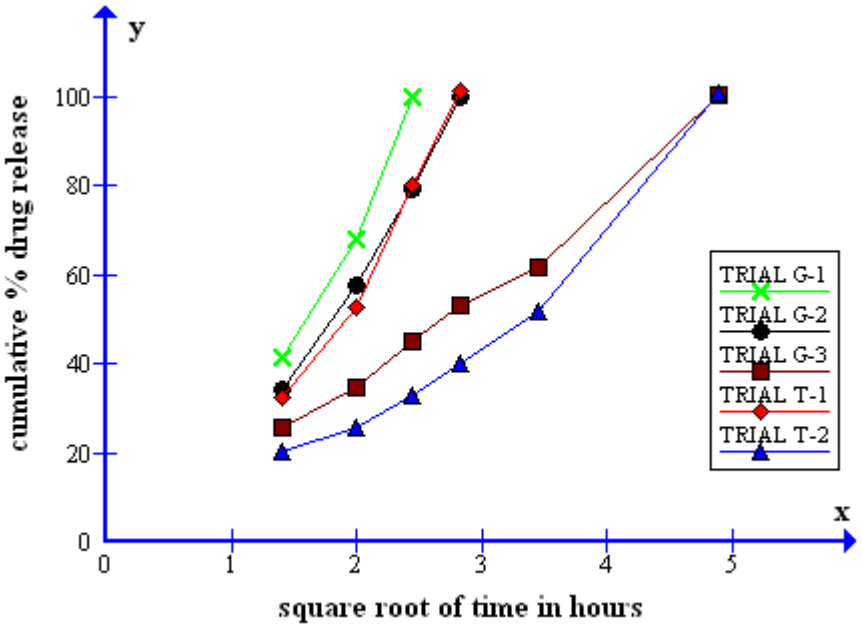


**Fig: 14 Higuchi model release kinetics of formulations G-1,G-2,G-3,T-1,T-2**

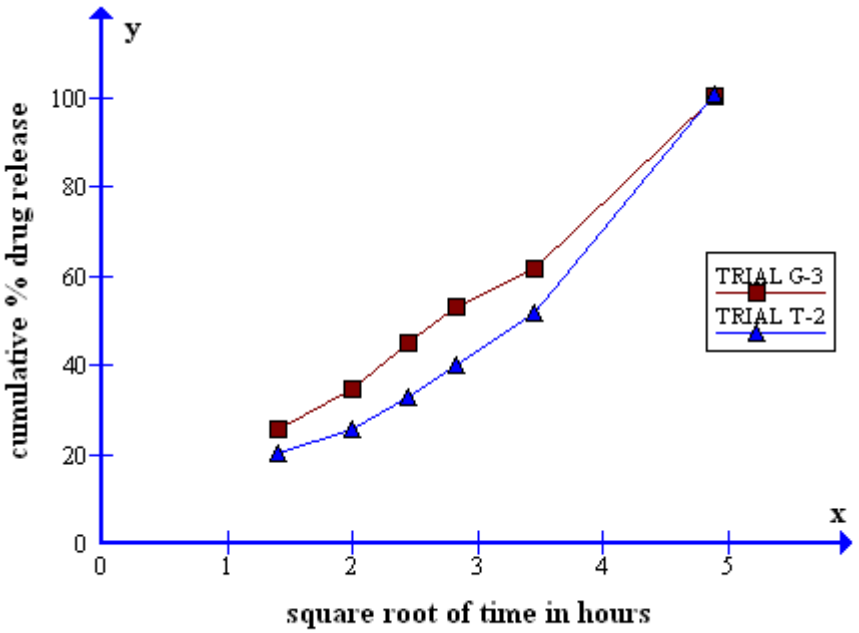


**Fig: 15 Higuchi Model release kinetics of formulations G-3, T-2**

**KORSMEYER-PEPPAS MODEL**

**Table: 9 Korsmeyer-Peppas Model Kinetics**

| SNO. | LOG OF TIME IN (hours) | LOG OF CUMULATIVE % DRUG RELEASE | | | | |
|---|---|---|---|---|---|---|
| | | TRIAL G- 1 | TRIAL G-2 | TRIALG- 3 | TRIAL T-1 | TRIAL T-2 |
| 1 | 0.301 | 1.617 | 1.535 | 1.407 | 1.511 | 0.391 |
| 2 | 0.602 | 1.832 | 1.761 | 1.539 | 1.721 | 0.849 |
| 3 | 0.778 | 1.999 | 1.898 | 1.652 | 1.903 | 1.177 |
| 4 | 0.903 | - | 1.998 | 1.723 | 2.005 | 1.445 |
| 5 | 1.079 | - | - | 1.788 | - | 1.848 |
| 6 | 1.381 | | - | 2.001 | - | 2.763 |

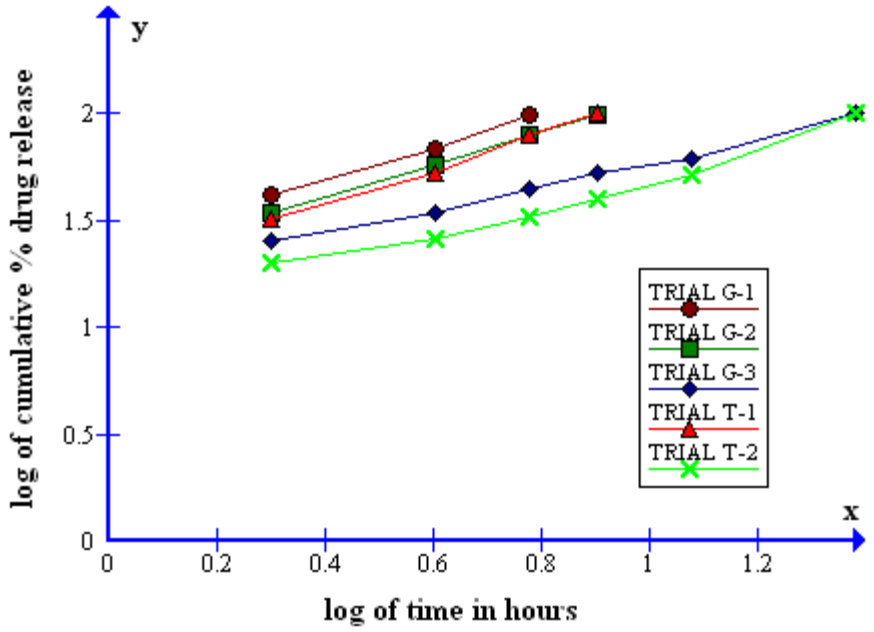


**Fig: 16 Kormeyer-Peppas model release kinetics of formulations G-1,G-2,G-3,T-1,T-2**

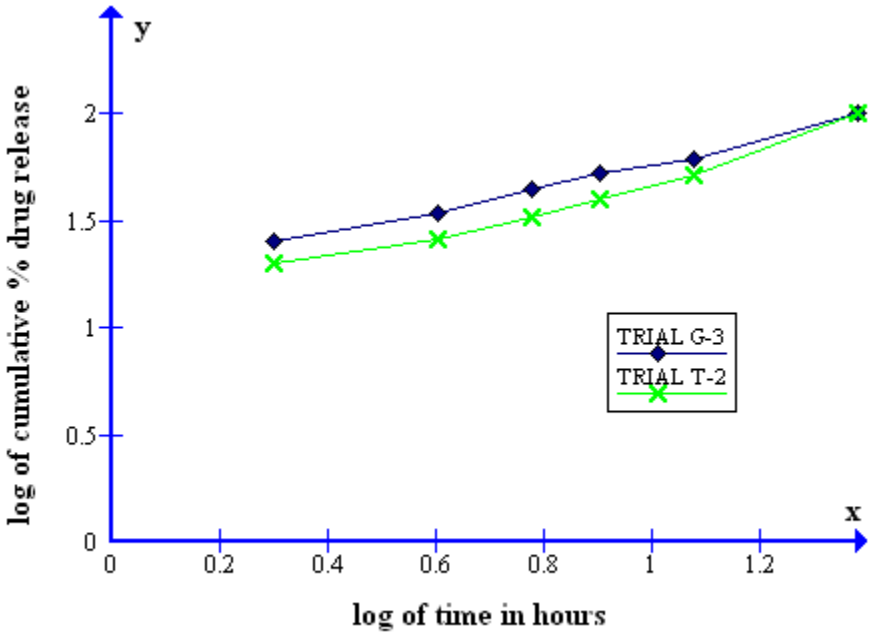


**Fig: 17 Korsmeyer-Peppas model release kinetics of formulationsG-3, T-2**

**Table: 10Diffusion Exponent 'n'**

| SNO. | FORMULATION | DIFFUSION EXPONENET 'n' |
|---|---|---|
| 1 | G-1 | 0.71 |
| 2 | G-2 | 0.75 |
| 3 | G-3 | 0.43 |
| 4 | T-1 | 0.69 |
| 5 | T-2 | 0.36 |

**FIRST ORDER RELEASE KINETICS**

**Table: 11First Order Release Kinetics**

| SNO. | TIME (hours) | LOG OF CUMULATIVE % DRUG REMAINING | | | | |
|---|---|---|---|---|---|---|
| | | TRIAL G- 1 | TRIAL G-2 | TRIALG- 3 | TRIAL T-1 | TRIAL T-2 |
| 1 | 2 | 1.767 | 1.815 | 1.871 | 1.837 | 1.905 |
| 2 | 4 | 1.503 | 1.622 | 1.815 | 1.687 | 1.873 |
| 3 | 6 | 0 | 1.313 | 1.741 | 1.325 | 1.831 |
| 4 | 8 | - | 0 | 1.672 | 0 | 1.781 |
| 5 | 12 | - | - | 1.585 | - | 1.687 |
| 6 | 24 | - | - | 0 | - | 0 |

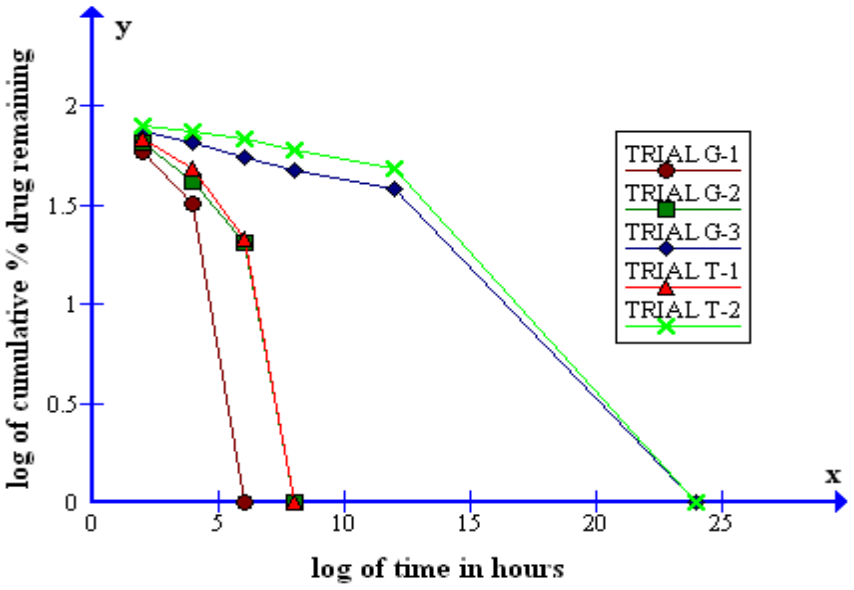


**Fig: 18 First order release kinetics of formulations G-1,G-2,G-3,T-1,T-2**

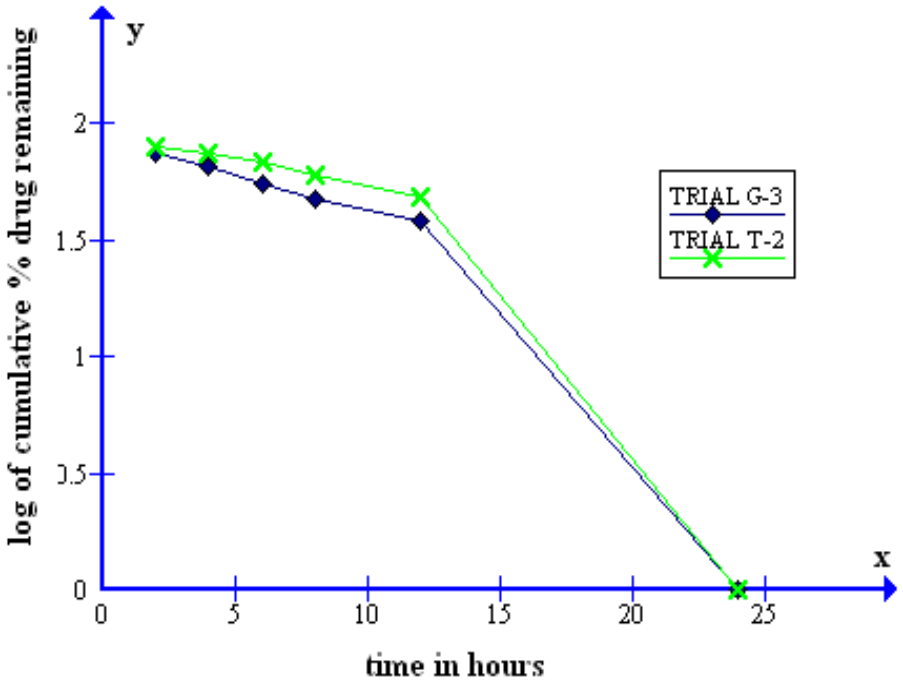


**Fig: 19 First order release kinetics of formulationsG-3,T-2**

**HIXSON-CROWELL CUBE ROOT KINETICS**

**Table: 12 Hixson-Crowell Cube Root Kinetics**

| SNO. | TIME (hours) | CUBE ROOT OF CUMULATIVE % DRUG REMAINING | | | | |
|---|---|---|---|---|---|---|
| | | TRIAL G- 1 | TRIAL G-2 | TRIALG- 3 | TRIAL T-1 | TRIAL T-2 |
| 1 | 2 | 3.882 | 4.027 | 4.207 | 4.097 | 4.315 |
| 2 | 4 | 3.171 | 3.474 | 4.028 | 3.65 | 4.211 |
| 3 | 6 | 0 | 2.739 | 3.805 | 2.766 | 4.077 |
| 4 | 8 | - | 0 | 3.61 | 0 | 3.926 |
| 5 | 12 | - | - | 3.376 | - | 3.652 |
| 6 | 24 | - | - | 0 | - | 0 |

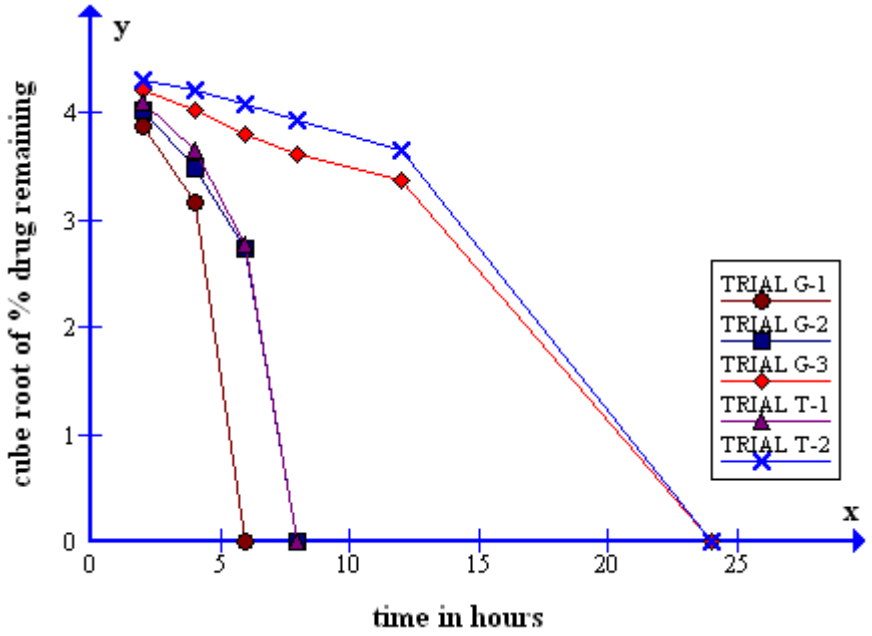


**Fig: 20 Hixson-Crowell Cube root release kinetics of formulations G-1,G-2,G-3,T-1,T-2**

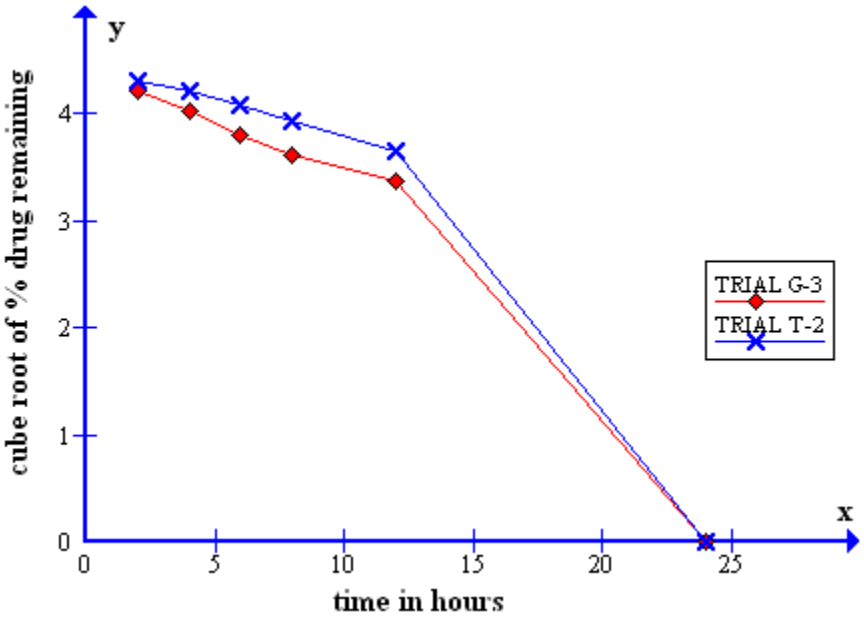


**Fig: 21 Hixson-Crowell Cube root release kinetics of formulations G-3,T-2**

**REGRESSION CO-EFFICIENT**

The classical linear regression model is the standard procedure for analyzing dependencies between variables that are measured on a metric scale. In the course of model estimation, it is common practice to assess the appropriateness of a single descriptive model for the problem under study with the help of the

coefficient of determination '$r^2$'. In empirical studies, the most important benefit of '$r^2$' is that it serves as a fast and easily interpretable measure for the goodness of fit of the estimated model. This advantage, however, comes with a big caveat, i.e. one may over-value the relevance of coefficients of determination, especially in the model selection process, and dedicate only minor interest to the substantive results of the analysis. '$r^2$' is no absolute indicator of goodness of fit; it is just a relative measure[5].

**Table: 13 Regreesion Co-efficient Values for Kinetic models**

| SNO. | FORMULATION | ZERO ORDER ($r^2$) | FIRST ODER ($r^2$) | HIGUCHI ($r^2$) | KORSMEYER-PEPPAS ($r^2$) | HIXSON-CROWELL CUBEROOT ($r^2$) |
|---|---|---|---|---|---|---|
| 1 | G-1 | 0.998 | 0.861 | 0.985 | 0.978 | 0.873 |
| 2 | G-2 | 0.999 | 0.943 | 0.993 | 0.984 | 0.858 |
| 3 | G-3 | 0.988 | 0.911 | 0.989 | 0.997 | 0.933 |
| 4 | T-1 | 0.997 | 0.822 | 0.991 | 0.982 | 0.857 |
| 5 | T-2 | 0.996 | 0.887 | 0.944 | 0.961 | 0.909 |

**STABILITY STUDIES**

After determining drug content, the tablets were charged for the accelerated stability studies according to ICH guidelines (40 ±2°C and 75 ± 5% RH) for a period of 2 months in stability chambers. The samples were taken out at 30 and 60 days and evaluated for the drug content, dissolution, related substances and physical parameters like hardness and friability.

**Table: 14 Stability Studies Data of Ideal Formulations**

| SNO. | FORMULATION | PROPERTIES | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | DRUG CONTENT (%) | DISSOLUTION (%) | | | | HARDNESS (%) | FRIABILITY (%) |
| | | | 2nd hour | 4th hour | 8th hour | 12th hour | | |
| | **After 1 month** | | | | | | | |
| 1 | G-3 | 103.4 | 26.44 | 36.26 | 55.14 | 61.19 | 7 | 0.05 |
| 2 | T-2 | 99.6 | 20.77 | 26.06 | 40.79 | 52.51 | 6 | 0.02 |
| | **After 2 month** | | | | | | | |
| 3 | G-3 | 98.7 | 25.68 | 35.5 | 54.47 | 60.8 | 8 | 0.02 |
| 4 | T-2 | 96.4 | 20.39 | 25.68 | 40.03 | 51.74 | 7 | 0.04 |

## DISCUSSION

### FT-Infrared spectroscopy to find out the compatibility of drug with polymer

The FT-IR was performed for drug, polymers, and physical mixture of drug and polymers. The spectra obtained from FTIR spectroscopy studies at wavelength from 2000 $cm^{-1}$ to 400 $cm^{-1}$. The different peaks of the samples are shown in the table7.1. From that it is evident that there is compatibility of the drug with polymer.

### Pre compression parameters

The prepared Aceclofenac granules were evaluated for angle of repose, bulk density, tapped density and compressibility index. The bulk densities of the granules were found to be in the range of 0.43 to 0.51 gm/ml. The tapped densities of the granules were found to be in the range of 0.48 to 0.62 gm/ml. The flow characteristics of the granules were assessed by determining their angle of repose. The low values of compressibility index (10.5 to 22.6) and the angle of repose (16°43' to 21°25') signifies good flow property of the granules for all the formulations. Thus ensuring homogenous filling of the dies.

### Post compression parameters

The tablets were evaluated for its hardness, weight variation, content uniformity and friability. Tablet hardness test is a measure of the cohesiveness of tablets and it plays a vital role for drug release. It is one of the official methods of the determination of tablets strength. Hardness must be controlled to ensure that the product is firm enough to withand handling without breaking or crumbling and not so hard that the disintegration time is unduly prolonged. The recommended value for tablet is 4 to 8 kg/cm2. The average hardness of the tablets to be in range was found within 7 to 8 kg/cm2 (for G-3 and T-2). The average weight variation of tablets was found within the limits of 7.5% (I.P.) Friability value which also affected by the hardness value of tablets should be in the range of 0.5 to 1% limits, which is the usual friability range of tablets. The friability of the prepared tablets was found less than 1% w/w. The uniformity of drug Aceclofenac present in tablets formulation ranged from 98.55% to 107.13%.It was found that the physicochemical parameters of the prepared tablets comply with the standards.

### *In vitro* drug release studies

The *in vitro* release of Aceclofenac from the prepared tablets was studied in phosphate buffer pH 6.8 for 24 hours. The results are presented in Figure 7.4. The cumulative percentage releases of Aceclofenac from the tablets were varied from to 99.94% to 101.27% depends on the drug polymer ratio for 24 hours. The Formulations G-1, G-2(guar gum) and T-1(tragacanth) have not shown any sustained release. Among the formulations G-3 and T-2 have showed maximum sustained release. This indicates that the combination of drug, polymer and other excipients probably ideal in Formulation G-3 and T-2.

**Selection of an ideal batch**

The best formulation from each batch was selected based on their physicochemical and release characteristics. Formulation G-3 and T-2 were selected as the best formulation and subjected to release kinetics studies.

**Release kinetics**

The *in vitro* release data obtained from FormulationsG-1, G-2, G-3, T-1 and T-2 was fitted to kinetic models. In case of zero order (Q = Q0 – K0t) the graph was plotted in cumulative percent of drug released Vs time, and in first order release kinetics (In Q = In Q0–K1t) the graph was plotted in log cumulative percent of drug remaining vs time. For Higuchi model kinetics (Q = K2 t1/2) the graph was plotted in cumulative percent of drug released vs square root of time, and for Korsmeyer-Peppas model (Q/Q0 = K tn) the graph was plotted in log cumulative percent of drug released vs log time. The release of Aceclofenac from the tablets was zero order diffusion controlled as indicated by higher $r^2$ values in zero order and Higuchi model. The n values obtained from the Korsmeyer-Peppas model gor G-3 and T-2 showed that the release mechanism was Fickian diffusion.

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