DESIGN AND DEVELOPMENT OF SUSTAINED RELEASE MATRIX TABLET OF DICLOFENAC SODIUM USING NATURAL POLYMER

Prakash Pawan1* and Kumar Nitin2

1Dept. of Pharmaceutics, Vivek College of Technical Education, Agri, Dhampur Road, Bijnor (U.P.), India
2Dept. of Pharmacy, Galgotias University, Noida (U.P.), India

ABSTRACT

In the present investigation an attempt has been made to study the formulation and evaluation of matrix tablets of diclofenac sodium using natural mucilage of Abelmoschus esculentus as a release retardant. The mucilage was extracted from the fruit of Abelmoschus esculentus using acetone. The mucilage was characterized for physiochemical and powder characteristics. The matrix tablets were formulated using different drug polymer ratio (1:0.25, 1:0.5, 1:0.75, 1:1). The developed formulations of tablets were evaluated for pre-compression and post-compression parameters. The results of pre-compression parameters like bulk density, tapped density, Carr’s index and Hausner’s ratio were found to be within the limits indicating good flow properties of the granules. Swelling index reveals that with increasing mucilage concentration there is increased swelling showing 51.34% for F4 at the end of 5 h where as for F1 and F2 it was around 43.43 % and 44.47 % respectively. In-vitro drug release for F4 formulation was found to be 98.97% at the end of 10 h. With increase in mucilage concentration the drug release from the matrix tablets got retarded. In-vitro drug release data obtained were fitted to various release models access the possible mechanism of drug release. All the formulations showed matrix (exponential model) as a best fit model and the release mechanism was found to be anomalous (non Fickian) transport mechanism. Therefore both diffusion and erosion mechanism was play role release from natural gum. Matrix tablets of diclofenac sodium using natural mucilage of Abelmoschus esculentus as a release retardant could be employed for retardant drug release. The matrix tablet prepared by Abelmoschus esculentus mucilage as drug polymer ratio of 1:1 (F4 formulation) provide better zero order release kinetics compared to marketed tablet Voveran SR 50mg.

Key words: Abelmoschus esculentus gum, Diclofenac sodium, Sustained release matrix tablet, Drug release kinetics

INTRODUCTION

The plant based polymers have been studied for their application in different pharmaceutical dosage forms like matrix controlled system, film coating agents, buccal films, microspheres, nanoparticles, viscous liquid formulations like ophthalmic solutions, suspensions, implants and their applicability and efficacy has been proven. These have also been utilized as viscosity enhancers, stabilisers, disintegrants, solubilisers, emulsifiers, suspending agents, gelling agents and bioadhesives, binders in the above mentioned dosage forms.1,2

Okra Abelmoschus esculentus L. (Moench), is an economically important vegetable grown in tropical and sub-tropical parts of the world. This crop is suitable for cultivation as a garden crop as well as on large commercial farms. It is grown commercially in India, Turkey, Iran, Western Africa, Yugoslavia, Bangladesh, Afghanistan, Pakistan, Burma, Japan, Malaysia, Brazil, Ghana, Ethiopia, Cyprus and the Southern United States. India ranks first in the world with 3.5 million tonnes (70% of the total world production) of okra produced from over 0.35 million ha land.3

Sustained Release provides the most desirable dosing regimens with effective pharmacokinetic profile and pharmacodynamic response in chronic pain management. This approach prevents the patient from experiencing pain intermittently through maintenance of consistent drug input and it may alleviate the variability involved in the administration of multiple doses per day. Thus Sustained Release Dosage Form of analgesic and antipyretic drug like Diclofenac sodium improves patient compliance and prevents the dramatic onset of analgesia seen with immediate release dosage form.4 Natural polysaccharides play a significant role in the formulation development of a new controlled release dosage forms as well as in human health care system.

In recent years, natural polysaccharides are growing rapidly and it continues to remain and important in the new formulation development of the controlled released dosage form. Natural polysaccharides are much safer than synthetic. They provide many applications in the formulation development of a new controlled release dosage form, such as binder, disintegrator, diluents and release modifier. Therefore, they needs a novel approach to enhance the use of natural polysaccharides in the formulation development of controlled released dosage form, because of the ease availability at an affordable price, high safety margin and higher productivity.5 Hence, the present study is aimed to enhance the use of natural plant based polysaccharide such as okra gum as a release modifier to develop Diclofenac sodium sustained release tablet.

MATERIALS AND METHODS

Materials

Diclofenac sodium was generously gifted by Unique Pharmaceuticals Ltd. Gujarat. Crude okra fruit purchased from local farmer and plant was authenticated in SVBP Agriculture University, Modipuram, Meerut (UP). Okra gum extracted from crude Abelmoschus esculentus was carried out at college laboratory (Pharmaceutics Research lab, VCTE, Bijnor (UP). Methanol and acetone were purchased from Ranbaxy Fine Chemical Ltd., New Delhi. Lactose, magnesium stearate and talc were purchased from S.D Fine chemicals, Mumbai.

Methods

Method of isolation and extraction of Okra gum:

About 2kg of fresh immature fruit of Abelmoschus esculentus were obtained from a local market. After removal of the seeds, the fresh immature fruits were sliced, homogenized and extracted with cold water containing 1% (w/v) sodium metabisulphate. The crude mucilage was centrifuged at 4000 rpm for 5 min and the gum was...
precipitated from the supernatant with acetone. The precipitated gum was washed several times with acetone; the obtained cream colored product was dried under vacuum in a desiccator. A light brown colored powder was obtained after complete removal of moisture. The dried gum was pulverized using end runner mill and screened through a 0.25 mm stainless steel sieve. This was stored in a well closed amber colored specimen bottle till ready for use.

**Physicochemical characterization of the gum:**

**Solubility**

One gram of gum from *Abelmoschus esculentus* was dissolved in 2 ml of distilled water.

**pH**

The pH of 1% w/v solution of the dry water soluble mucilage/polysaccharide in distilled/demineralized water was measured using a calibrated digital pH meter at room temperature. The study was conducted in triplicate to ensure the accuracy.

**Water content**

Gravimetric method was used. Ten grams of the gum powder was accurately weighed and dried at 105°C for 5 hours. The sample was weighed and weight loss calculated.

**Flow property of the gum powder**

The bulk characterization of the dry water soluble mucilage/polysaccharide such as Angle of repose, Bulk and Tapped bulk density, Carr's index and Hausner's ratio were determined using conventional techniques.

**Particle size distribution**

The particle size distribution of the mucilage/polysaccharide was carried out using conventional techniques.

**Swelling ratio**

In this study 1 g of dry gum powder was placed in a 100-ml stoppered graduated cylinder. The initial bulk volume of the dry mucilage was measured. 2 ml of alcohol (95%) was added for good dispersion and then distilled/demineralized water was added to sufficient quantity to yield 100-ml of uniform dispersion. The viscous solution was added at room temperature and the sediment volume of the swollen mass was noted after 24 hr. The swelling ratio was calculated by determining the ratio of swollen volume to the initial bulk volume using the formula:

\[
S = \frac{V2-V1}{V1}
\]

Where;

- \(S\) = swelling index
- \(V1\) = volume occupied by the mucilage prior to hydration
- \(V2\) = volume occupied by the mucilage after hydration.

**Rheological properties**

Viscosity determinations were made in a Brookfield viscometer, measuring shear at 2, 4, 10 and 20 r.p.m. versus viscosity.

**Infrared spectra of the gum**

A potassium bromide disc of each of the dried purified mucilages was prepared, and the infrared spectra recorded (Shimadzu FTIR 8700) between 4000 and 650 cm\(^{-1}\).

**Characteristics and evaluation of granules:**

**Angle of repose**

The angle of repose of granules was determined by the funnel method. The accurately weight granules were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The granules were allowed to flow through the funnel freely on to the surface\(^7\). The diameter of the granules cone was measured and angle of repose was calculated using the following equation.

\[
\tan \theta = \frac{h}{r}
\]

Where, \(h\) = height of the powder cone, \(r\) = radius of the powder cone.

**Bulk density**

Both loose bulk density (LBD) and tapped bulk density (TBD) was determined. A quantity of 2 gm of granules from each formula, previously shaken to break any agglomerates formed, was introduced into to 10 ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted\(^8\). LBD and TBD were calculated using as the following equations:

- LBD = Weight of the granules / Untapped Volume of the packing
- TBD = Weight of the granules / Tapped Volume of the packing

**Compressibility index**

The Compressibility Index of the granules was determined by Carr’s (compressibility) index. It is a simple test to evaluate the LBD and TBD of a granules and the rate at which it packed down\(^9\). The formula for Carr’s Index is as below:

\[
\text{Carr’s index} = \frac{(\text{TBD-LBD})}{\text{TBD}} \times 100
\]

**Preparation of sustained release matrix tablets:**

Matrix tablets containing Diclofenac sodium were prepared by wet granulation technique using variable concentrations of okra mucilage and lactose as filler. Different tablets formulations were prepared by wet granulation method. All the powders were passed through 60 mesh sieve. Required quantity of drug, and lactose were mixed thoroughly. Then, polymer dissolve in granulating agent (isopropyl alcohol) was added slowly with uniform mixing the get a wet mass. The wet mass was passed through sieve no 10 to 11 hrs in try dryer. The dried granules were passed through sieve no.22, after blending with lubricants were compressed into tablet compression machine using tablet compression machine. Each tablet contained 50 mg of Diclofenac sodium and other pharmaceutical ingredients as listed in table 4.

**Evaluation of tablets:**

**Weight variation test**

To study weight variation twenty tablets of the formulation were weighed using a Essae electronic balance and the test was performed according to the official method. Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation\(^10\).

**Drug content**

Five tablets were weighed individually and powdered. The powder equivalent to average weight of tablets was weighed and drug was extracted in Phosphate buffer pH 6.8, the drug content was determined measuring the absorbance at 276 nm after suitable dilution using a UV- Vis double beam spectrophotometer Shimadzu 1800, Japan\(^11\).

**Hardness**

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Pfizer hardness tester. It is expressed in kg/cm². Three tablets were randomly picked and hardness of the tablets was determined\(^12\).
Thickness
The thickness of the tablets was determined by using Vernier calipers. Five tablets were used, and average values were calculated.

Friability test
The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed and transferred into friabilator. The friabilator was operated at 25rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again. The % friability was then calculated by:
% F = 1 - (loss in weight/initial weight) 100

% Friability of tablets less than 1% are considered acceptable.

In Vitro dissolution studies
The in vitro release of Diclofenac sodium from the formulated tablets was carried out in Tablet dissolution tester USP- Labindia DS 8000 using 900 ml of dissolution medium maintained at 37.0 ±0.5°C and a stirring rate of 100 rpm. Six tablets from each formulation were tested individually in phosphate buffer (pH 1.2) for the first 2 h and in simulated gastric fluid (pH 6.8) for the following 10 h. At every 1 h interval, samples of 5 ml were withdrawn from the dissolution medium and replaced with fresh medium to maintain the volume constant. After filtration and appropriate dilution, the amount of DS resent in each sample was determined spectrophotometrically at 276 nm.

Kinetics of drug release:
To examine the drug release kinetics and mechanism, the cumulative release data were fitted to models representing zero order (Q v/s t), first order [Log(Q0-Q) v/s t], Higuchi’s square root of time (Q v/s t1/2 ) and Korsmeyer Peppas double log plot (log Q v/s log t) respectively, where Q is the cumulative percentage of drug released at time t and (Q0-Q) is the cumulative percentage of drug remaining after time t. In short, the results obtained from in vitro release studies were plotted in four kinetics models of data treatment as follows:
- Cumulative percentage drug release Vs. Time (zero order rate kinetics)
- Log cumulative percentage drug retained Vs. Time (first order rate kinetics)
- Cumulative percentage drug release Vs. T (Higuchi’s classical diffusion equation)
- Log of cumulative percentage drug release Vs. log Time (Peppas exponential equation)

Accelerated stability studies of optimized matrix tablets:
The promising matrix tablet was tested for a period of three months for accelerated condition (Temperature of 40°C and Relative Humidity of 75%RH) and drug content and other parameter was estimated.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Parameters</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Solubility</td>
<td>Slightly soluble in water</td>
</tr>
<tr>
<td>2</td>
<td>Odour</td>
<td>Characteristics</td>
</tr>
<tr>
<td>3</td>
<td>Taste</td>
<td>Mucilaginous</td>
</tr>
<tr>
<td>4</td>
<td>Appearance</td>
<td>Amorphous</td>
</tr>
<tr>
<td>5</td>
<td>Percentage yield</td>
<td>1.2%</td>
</tr>
</tbody>
</table>
| 6      | Identifications | a) mounted in 96% ethanol
b) mounted in ruthenium red |
| 7      | pH (1% solution) | 4.91 |
| 8      | % LOD      | 2.3% |
| 9      | Swelling index | 80.23 |
| 10     | Ash value  | 5.12% |
| 11     | Viscosity (1% solution) at room Temperature | 206 cps |

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Parameters</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Average particle size</td>
<td>48.00 μm</td>
</tr>
<tr>
<td>2</td>
<td>Angle of repose</td>
<td>26.32</td>
</tr>
<tr>
<td>3</td>
<td>Bulk density</td>
<td>0.54 gm/cm3</td>
</tr>
<tr>
<td>4</td>
<td>Tapped density</td>
<td>0.73 gm/cm3</td>
</tr>
<tr>
<td>5</td>
<td>Carr index</td>
<td>26.02</td>
</tr>
<tr>
<td>6</td>
<td>Hausner’s ratio</td>
<td>1.35</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Granule batch</th>
<th>Angle of Repose(°)</th>
<th>Bulk density (gm/ml)</th>
<th>Tapped density gm/ml</th>
<th>Compressibility (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>f1</td>
<td>26.23</td>
<td>0.496</td>
<td>0.620</td>
<td>26.10</td>
</tr>
<tr>
<td>2</td>
<td>f2</td>
<td>26.69</td>
<td>0.469</td>
<td>0.582</td>
<td>19.42</td>
</tr>
<tr>
<td>3</td>
<td>f3</td>
<td>27.10</td>
<td>0.529</td>
<td>0.604</td>
<td>12.42</td>
</tr>
<tr>
<td>4</td>
<td>f4</td>
<td>28.45</td>
<td>0.532</td>
<td>0.611</td>
<td>12.93</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Ingredient (mg/tab)</th>
<th>f1</th>
<th>f2</th>
<th>f3</th>
<th>f4</th>
<th>f5</th>
<th>f6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diclofenac sodium</td>
<td>50mg</td>
<td>50mg</td>
<td>50mg</td>
<td>50mg</td>
<td>50mg</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Okra gum</td>
<td>12.5mg</td>
<td>25mg</td>
<td>37.5mg</td>
<td>50mg</td>
<td>50mg</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Lactose</td>
<td>272mg</td>
<td>260mg</td>
<td>247mg</td>
<td>235mg</td>
<td>8mg</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Talc</td>
<td>8.5mg</td>
<td>8mg</td>
<td>8.5mg</td>
<td>8mg</td>
<td>8mg</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Mg. Stearate</td>
<td>7mg</td>
<td>7mg</td>
<td>7mg</td>
<td>7mg</td>
<td>7mg</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Weight of tablet</td>
<td>350mg</td>
<td>350mg</td>
<td>350mg</td>
<td>350mg</td>
<td>350mg</td>
<td></td>
</tr>
</tbody>
</table>
Table 5 Evaluation data for physical parameters of matrix tablets

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Formulation Batch</th>
<th>Weight variation test (mg)</th>
<th>Friability (%)</th>
<th>Hardness (Kg/cm²)</th>
<th>Drug content (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>f1</td>
<td>0.347±0.005</td>
<td>0.85</td>
<td>7.5</td>
<td>97.91</td>
</tr>
<tr>
<td>2</td>
<td>f2</td>
<td>0.348±0.004</td>
<td>0.79</td>
<td>10</td>
<td>98.89</td>
</tr>
<tr>
<td>3</td>
<td>f3</td>
<td>0.348±0.005</td>
<td>0.81</td>
<td>12</td>
<td>98.38</td>
</tr>
<tr>
<td>4</td>
<td>f4</td>
<td>0.350±0.005</td>
<td>0.69</td>
<td>12.5</td>
<td>99.80</td>
</tr>
</tbody>
</table>

Table 6 Summary of physical properties of optimized f4 formulation before and after accelerated study

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before Stabilities Studies</th>
<th>After Stabilities Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness (Kg/cm²)</td>
<td>12.5</td>
<td>12.8</td>
</tr>
<tr>
<td>Friability (%)</td>
<td>0.69</td>
<td>0.67</td>
</tr>
<tr>
<td>Drug content (%)</td>
<td>99.80</td>
<td>99.60</td>
</tr>
</tbody>
</table>

Figure: 1 Particle size distributions of dry Okra gum powder

Figure: 2 IR spectrum of okra gum

Figure 3 Graph for Zero order kinetic models of formulation f1, f2, f3 and f4.
Figure: 4 Graph for First order kinetic release model of formulation f1, f2, f3 and f4

Figure: 5 Graph for Higuchi model of formulation f1, f2, f3 and f4

Figure: 6 Graph for Korsmeyer-Peppas model of formulation f1, f2, f3 and f4.
RESULTS
Characterization of okra gum
The purified Okra gum was characterized for physicochemical, rheological and for powder flow characteristics (see table 1 and 2). The particle size distribution has shown in figure 1. The FTIR study of the dry water soluble mucilage/polysaccharide obtained from different solvents were performed to ensure the stability while using different solvents for extraction. The spectra of the dry water soluble mucilage/polysaccharide are shown in Fig. 2
Pre-compression study and evaluation of tablet parameter
The various characteristics of granules are listed in table 3. The results from different physical parameters of tablet are shown in table 5.
Mathematical models
Zero order release kinetics
In its simplest form, zero order release can be represented as
\[ Q = Q_0 + K_0 t \]
Where Q is the amount of drug released or dissolved (assuming that release occurs rapidly after the drug dissolves), Q0 is the initial amount of drug in solution (it is usually zero), and K0 is the zero order release constant. The plot made: cumulative% drug release vs. time (zero order kinetic models) was shown in Figure: 3.
First order release kinetics
The rate laws predicted by the different mechanisms of dissolution both alone and in combination, have been discussed by Higuchi. However, the earliest equation expressing dissolution rate in a quantitative manner was proposed by Noyes and Whitney as:-
\[ \frac{dC}{dt} = k (C_s - C_t) \]
Where \( \frac{dC}{dt} \) is the rate of change in concentration with respect to time, and k is the rate constant. The integrated form of the equation is:
\[ \ln \left( \frac{C_s}{C_s - C_t} \right) = kt \]
\[ \log C = \log C_0 - \frac{kt}{2.303} \]
Where, C0 is the initial concentration of drug and K is first order constant.
The plot made: log cumulative of % drug remaining vs. time shown in figure 4.
Higuchi Model
Higuchi was the first to derive an equation to describe the release of a drug from an insoluble matrix as the square root of a time-dependent process based on Fickian diffusion.
\[ \frac{Mt}{M_N} = Ktn \]
Where, Mt is the amount of drug released in time t, D is the diffusion coefficient, S is the solubility of drug in the dissolution medium, N is the porosity, A is the drug content per cubic centimeter of matrix tablet, and KH is the release rate constant for the Higuchi model. The plot made: cumulative % drug release vs. square root of time shown in figure 5.
Korsmeyer-Peppas Model
Korsmeyer et al (1983) 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:
\[ Mt/M_N = Ktn \]
Where $Mt / MS$ is fraction of drug released at time $t$, $k$ is the rate constant and $n$ is the release exponent. The in vitro drug release modal of Korsmeyer-Peppas show the plot made: log cumulative % drug release vs. log time shown in figure 6.

**Hixson-Crowell cube-root Model**

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. For a drug powder consisting of uniformly sized particles, it is possible to derive an equation that expresses the rate of dissolution based on the cube root of the particles.

$$
\frac{Q0}{1/3 - Qt} = KHC t
$$

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 plot made: cube root of drug % remaining in matrix vs. time shown in figure 7.

**Swelling index**

Swelling index of tablets prepared from *Abelmoschus esculentus* mucilage are reported in figure 8. 

**Accelerated stability studies of optimized matrix tablets**

Summary of physical properties of optimized f4 formulation before and after accelerated study reported in table 6.

**DISCUSSION**

In the present work, an attempt has been made to prepare sustained release matrix tablets of Diclofenac sodium by natural polymer *Abelmoschus esculentus* using lactose as filler by wet granulation method.

**Extraction and characterization of mucilage**

The mucilage was successfully extracted from *Abelmoschus esculentus* for pharmaceutical use. The product extracted was acceptable with characteristic, odour, muclaginous taste and coarse powder aspects. The pH of 1% w/v solution of the mucilage of *Abelmoschus esculentus* in distilled water was found 4.91. The viscosity of 1% mucilage solution of *Abelmoschus esculentus* was found to be 206 cps. The swelling index of mucilage powder was found to be 80.23.

In powder characterisation studies, angle of repose, bulk density, tapped density, cars index and hausners ratio were performed and results was found 26.23, 0.54 gm/cm3, 0.73 gm/cm3, 26.02.

**Evaluation of Physical characterization:**

**Hardness test**

The hardness of tablets was found to in the ranges of 7.5 to 12.5 kg/cm2 but matrix tablets (f4) contain okra gum with ratio as (1:1) produce highest hardness as 12.5 kg/cm2.

**Friability test**

The % weight loss in friability test was found to be less than 1% (0.69 to 0.85%) indicate tablets can withstand the mechanical shock or during handling.

**Weight Variation Test**

The average weight of tablets was found to be 350 mg for all batches and % deviation within specified limits. Overall the all prepared formulation was good quality with regard to drug content.

**Drug Content Uniformity**

Good uniformity in drug content was found among different batches of tablets and percentage of drug content was more than 96%. Hence it complies with official specification. In formulation f4 the drug content was found to be 99.80% which indicate better drug content uniformity among all formulation.

**Evaluation of swelling index of Matrix tablets**

The swelling behavior indicates the rate at which tablets absorb the water from dissolution media and swells. Swelling of matrix tablets increases with respect to time because weight gain by tablets was increased proportionally with rate of hydration up to 6 hrs and matrix appeared swollen almost from the beginning and a viscous gel mass was created after contact with water later on swelling were decreases due to dissolution of outermost gelled layer of tablets. The swelling index of all formulation increases as increase the concentration of gum in each formulation reported in (Figure 8). Swelling index of tablets prepared from *Abelmoschus esculentus* mucilage (F3, F4) with ratio as (1:0.75, 1:1) resulted as better swelling behaviour with respect to concentration. It has observed that drug release decreases with increasing concentration of gum and swelling index. The reason attributed to this fact is formation of thick gel layer by matrices around tablets that delays diffusion and release drug.

**In vitro drug dissolution study**

All formulations showed very low drug release in 0.1N HCl (pH 1.2). Sustained, but complete drug release was displayed by all formulations in phosphate buffer (pH 6.8).

**In vitro dissolution data of formulation (F1 to F4) reported in (Figure: ).When matrices containing swellable polymers are exposed to dissolution medium, tablet surface becomes wet and hydrated to form a gel layer. The initial release of drug from these matrices occurs by the drug dissolution in the water penetrated into the matrix. The overall drug release from these matrices is governed by hydration, gel layer formation and drug diffusion into the gel layer and to the dissolution media.**

Polymer erosion also plays a major role in releasing drug from these matrices. These considerations indicate that hydrophilic polymers have the potential to sustain the release of drug from matrix tablets. The release of drug is retarded as concentration of gum increases in all formulation. In order to investigate the effect of polymer type and percentage on drug release profile, different formulations containing various percentages of *Abelmoschus esculentus* mucilage which is used as a retarding release of drug in controllable manners up to 10 hrs.

The formulation (F1 to F4) containing *Abelmoschus esculentus* mucilage ratio as (1:0.25, 1:0.5, 1:0.75, 1:1) were able to sustain the drug release up to 10 hrs with percentage drug release as (95.36%, 98.90%, 97.35%, 98.97%) respectively. indicate that rate of release decreases as the concentration of gum increases with decreasing swelling index of matrix tablets. By increasing the polymer percentage, a viscous gel layer is formed, resisting to erosion and the diffusion of the drug is controlled primarily by the gel viscosity. The viscosity of gum solutions strongly increases with increasing concentration of the gum. The behavior is attributable to the intermolecular interaction or entanglement, increasing the effective macromolecule dimensions and molecular weight. As a result of rheology of hydrated product, the swollen particles coalesce. This results in a continuous viscoelastic matrix that fills the interstices, maintaining the integrity of the tablet, and retarding further penetration of the dissolution medium. In-vitro drug release profile with swelling behavior the formulation (F4) as optimized for further studies. Optimized matrix tablets (F4) shows linear from hydrophilic matrices have been synchronization between swelling and erosion of gum and maintain gel layer.
Determination of the Release Kinetics:
The in vitro drug release data was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic equations, Higuchi’s and Korsmeyer’s models in order to determine the mechanism of the drug release. The linear regression analysis of all the fabricated tablets shows as R² values. When the data were plotted according to the first-order equation for formulations (F1 to F4) prepared by okra mucilage showed a fair linearity with regression (R²) values between (0.92 to 0.97) clearly indicate that drug was release as per near first order. When the regression coefficient values of zero order and first order plots were compared it was observed that the R² values of zero order plots were in the range of 0.79 to 0.96 indicating drug release was not found to follow zero order kinetics but optimized formulation f4 follow near zero order kinetics which have R² value 0.968. Figure-5 shows the percent drug released versus square root of time plots. It is notable that the R² values of the linear regressions for Higuchi plots were found to be (0.89 to 0.97) for formulation (f1 to f4) prepared by okra gum indicating that the data fits the near Higuchi model and the drug release was found to be partially controlled by diffusion process. When the in vitro dissolution data was fitted to exponential model, the ‘r’ values were found to be in the range of 0.95 and 0.99 in most of the formulations, indicating the data fits the exponential model well. The slope (n) values of exponential equation were found to be >0.45 and <0.82 indicating drug release is governed by non-Fickian diffusion mechanism.

Evaluation of Stability of tablet
The optimized formulation as (F4) was further evaluated for Accelerated stability studies as per ICH guidelines mention earlier. It was suggested that there was no significant changes in physical parameters like hardness, thickness, weight variation, content uniformity (Table 6).

CONCLUSION
Result of the present study demonstrates that natural gum based material successfully employed for formulating the sustained release matrix tablets of Diclofenac Sodium. It is evident that the investigated sustained release matrix of Abelmoschus esculentus mucilage at 10-15% concentration was capable of prolonging the release of drug for 10 hrs. The mechanism of drug release was observed to be following Korsmeyer-Peppas model (Anomalous transport) and zero order kinetics therefore both diffusion and erosion effect for sustained drug release. The drug content was uniform in all the formulations of tablets prepared. The low values of standard deviation indicate uniform distribution of drug within the matrices. Infrared spectroscopic studies indicated that the drug is compatible with the polymer. The drug-polymer ratio was found to influence the release of drug from the formulations. As the polymer level is increased, the drug release rates were found to be decreased. Drug release was found to follow near zero order kinetics and mechanism of drug release was observed to be following Korsmeyer-Peppas model (Anomalous transport) both diffusion and erosion effect for sustained drug release.

REFERENCES

Source of support: Nil, Conflict of interest: None Declared