**Formulation and evaluation of sustained release matrix tablets of diclofenac sodium using natural polymer (Linum usitatissimum seed mucilage)**

**Abstract:**

The main accusative of the present work was to develop sustained release matrix tablets of Diclofenac sodium for maintaining therapeutic blood or tissue levels of the drug for extended period of time with minimized local or systemic adverse effects. In the present study, Polysaccharide mucilage derived from the seeds, Linum usitatissimum (family Linaceae) was investigated as sustained release matrix forming material in tablet formulations. Mucilage extracted from seeds was subjected to physicochemical characterization. Matrix tablets were prepared by wet granulation technique using isopropyl alcohol as a granulating agent in different drug: polymer ratios. Compressed tablets were evaluated for uniformity of weight, content of active ingredient, friability, hardness, thickness and in vitro dissolution using paddle method. All the formulations showed compliance with pharmacopeial standards. Tablets prepared with Hydroxypropyl methylcellulose (HPMC 50cps) and Xanthan gum as matrix forming material for the comparative study. With increasing the percentage of natural polymer, release rate decreased, though drug release pattern was mainly dependent on the type of polymer and follows zero order kinetics. The dissolution study proved that the Linum usitatissimum seeds mucilage can be used as a matrix forming material for making thrice daily Sustained release matrix tablets of Diclofenac sodium.The objective of present study was to isolate and investigate the suitability of the linseed mucilage as a sustained release matrix material to develop controlled release tablets of the selected model drug Diclofenac sodium in comparison with established polymers like xanthan gum and HPMC.

**Introduction:**

Drug products designed to reduce the frequency of dosing by modifying the rate of drug absorption have been available for many years. Regular research is going on infield of use of natural occurring biocompatible polymeric material in designing of dosage form for oral controlled release administration. The advantages of natural plant-based excipients include low cost, natural origin, free from side effects, biocompatible, bioacceptable, renewable source; environmentally friendly processing, local availability, better patient tolerance as well as public acceptance. They improve the national economy by providing inexpensive formulations to people, using locally available materials. Natural polysaccharides and dried mucilage have been widely explored as emulsifying, suspending, binding and disintegrating agent and as sustained-release matrix by the pharmaceutical industry. Natural polymers suffer from certain limitations like, non-uniformity in yield and quality. There are number of methods are available to ensure their yield and uniformity of the product. Natural polymers like alginate, gelatin, guar gum, xanthan gum, locust been gum, gellan gum have been utilized in variety of formulations like gastroretentive, colon specific drug delivery system etc.

Oral route of drug administration is the most appealing, convenient, significant and popular route for the delivery of drugs owing to ease of swallowing, self-medication, and most economic. Tablets are the most popular and preferred oral formulation available in the market because of its ease of manufacturing, convenience in administration, accurate dosing, stability compared with oral liquids and because it is more tamperproof than capsules. The primary benefits of a sustained release dosage forms compared to a conventional dosage form, is maintenance of constant plasma drug concentration and therefore maintains uniform therapeutic effect.

Over the past two decades, sustained release drug delivery systems have made significant progress in terms of clinical efficacy and patient compliance. Drug-release-retarding polymers are the key performers in such systems. Regarding this, researchers investigated various natural, semi-synthetic and synthetic polymeric materials. Matrix system is most commonly used method for modulating the drug release in oral controlled drug delivery to obtain a desirable drug release profile, cost effectiveness and broad regulatory acceptance. Matrix devices, due to their chemical inertness, drug embedding ability and drug release character, have gained steady popularity for sustaining the release of a drug.

Various approaches have been used to obtain controlled drug release, but hydrophilic matrix is recognized as the simplest and is the most widely used. Upon ingestion of a hydrophilic matrix tablet drug release results initially from swelling which causes a gel layer to form on the tablet surface. This gel layer retards further ingress of fluid and subsequent drug release. The swelling of the polymer matrix very often occurs simultaneously with erosion, and both of them contribute to the overall drug release rate. Hydrophilic matrices from natural polysaccharide gums such as xanthan gum, guar gum and karaya gum have been shown to provide varying degrees of sustained release of medicaments. Both synthetic and natural polymers have been investigated extensively for this purpose.

**Pharmacognostic study of flax seeds:**

 Flaxseed, also known as linseed, is derived from the flax plant (Linum usitatissimum), of the family Linaceae, which is cultivated worldwide for its fiber and oil. Flaxseed contains 6% mucilage or soluble fibers, insoluble fibers 18%, 25% proteins, and 30-40% oil, with alpha-linolenic acid (ALA) making up about 50- 60% of the total fatty acids. The lignan constituent of flaxseed (but not its oil) possesses in vitro anti-oxidant and possible estrogen receptor agonist/antagonist properties, prompting hypotheses on its utility in the treatment of breast cancer, prostate cancer inflammatory bowel disease, lupus nephritis and type 2 diabetes.

**Common name**: Flax

**Latin name**: Linum usitatissimum,

**Synonyms:** Linseed, Common Flax, Flax Weed,

Lint Bells, and Toad Flax

**Family:** Linaceae

**Components of flax seed**: Alpha-linolenic acid (ALA), cyanogenic glycosides (linamarin, linustatin, neolinustin), unsaturated fatty acids (linolenic acid, linoleic acid, oleic acid), soluble flaxseed fiber mucilage (d-Xylose, L-Galactose, LRhamnose, d-galacturonic acid), lignans (secoisolariciresinol diglycoside (SDG)), monoglycerides, triglycerides, free sterols, sterol esters, hydrocarbons (protein), balast, phenylpropane derivatives.

**Habitat**: The plant is native to the temperate regions of Europe and Asia.

**Description**: Flax is a small, herbaceous, annual plant, growing to 1, 2 meters tall. It has erect, smooth stem and glaucous green, linear leaves. Flowers are small, five-petalled, pale blue or bright red in color. Fruits are round, dry capsules filled with brown seeds.

**Parts used:** Seed

**Useful components:** Fixed oil, mucilage, proteins, linamarin, omega-3 fatty Acids

**Medicinal use:** Flax seeds are considered to be extremely beneficial for different types of ailments.

**Health-promoting properties of flax**

Flax oil, flax seeds, and the omega-3 fatty acids they contain are good for health. Here are some of the ways flax helps in promoting the health:

1. Flax promotes cardiovascular health. The ultra-high levels of omega-3 fatty acids lower LDL (bad) cholesterol levels. Fish oils and algae are also good sources of essential fatty acids.

2. Flax promotes colon health. It has anti-cancer properties and, as a natural lubricant and a rich fiber source, it lowers the risk of constipation.

3. Flax supplements can boost immunity. One study showed that school children supplemented with less than a teaspoon of flax oil a day had fewer and less severe respiratory infections than children not supplemented with flax oil.

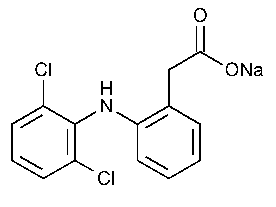
4. Flax provides fats that are precursors for brain building. This is especially important at the stage of life when a child's brain grows the fastest, in uterus and during infancy. A prudent mom should consider supplementing her diet with a daily tablespoon of flax oil during her pregnancy and while breastfeeding.

5. Flax promotes healthy skin. dry skin or eczema conditions can be treated.

6. Flax may lessen the severity of diabetes by stabilizing blood-sugar levels.

7. Flax fat can be slimming. Fats high in essential fatty acids, such as flax, increase the body's metabolic rate, helping to burn the excess, unhealthy fats in the body.

**Active pharmaceutical ingredient (Diclofenac):**

Diclofenac sodium is a well-known representative of non-steroidal anti-inflammatory drugs, widely used to control pain and inflammation of rheumatic and non-rheumatic origin. The conventional tablets make the drug immediately available for absorption in upper GI tract resulting local GI toxicity varying from minor gastric discomfort to ulceration and bleeding of the mucosa. It is well documented that the GI toxicity is not only caused by the inhibition of the prostaglandin synthesis, but is probably also due to direct contact of the drug with the mucosa. In addition, due to the rapid systemic clearance of this drug, repeated daily dosing of 3 to 4 times a day is required in maintenance therapy that influences patient compliance. Sustained release formulations of diclofenac sodium are thus warranted to promote patient compliance and to reduce upper GI toxicity to some extent.

Diclofenac Sodium [2- [(2, 6- dichlorophenyl) amino] benzene acetic acid monosodium salt] is a drug which is sparingly soluble in water and freely soluble in organic solvent like methanol. Anti-inflammatory and antipyretic action is through an unknown mechanism that may involve inhibition of prostaglandin synthesis. Pharmacokinetic profile of Diclofenac sodium is after oral administration, diclofenac is rapidly and almost completely absorbed. Absorption is delayed by food. It is highly protein bound. Diclofenac undergoes first-pass metabolism, with 60% of unchanged drug reaching systemic circulation. About 40% to 60% is excreted in the urine; the balance is excreted in the bile. Diclofenac sodium is used as analgesic, antipyretic, anti-inflammatory and approved in the United States for the longterm symptomatic treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. Oral form of diclofenac sodium is contraindicated in the patients having hypersensitivity, hepaticporphyria, history of asthma, utricaria, late pregnancy, breast feeding and cautious in case of peptic ulcer. Diclofenac sodium have a few side effects like anxiety, depression, dizziness, insomnia, hypertension, edema, taste disorder, transient stinging, abdominal pain or cramps, bleeding, colitis, acute renal failure, nephritic syndrome, heart failure.

**Method of isolation of flax seed mucilage:**

**Aim:** To separate the flax seed mucilage from flax seeds.

**Requirements:** flax seeds, acetone, muslin cloth, hot air oven, sieves.

**Procedure**: The seeds were washed with water to remove dirt and debris, and dried. The dried seeds were crushed and powdered in ball mill. To 20g of seed powder, 200ml of cold distilled water was added and slurry was prepared. The slurry was poured into 800ml of boiling distilled water. The solution was boiled for 20 minutes under stirring condition in a water bath. The resulting thin clear solution was kept overnight so that most of the proteins and fibers settled out. The material was squeezed from an eight-fold muslin cloth bag to remove the marc from the solution. Acetone was added to the filtrate to precipitate the mucilage in a quantity of three times the volume of the total filtrate. The mucilage was separated, dried in an oven at a temperature < 50 °C, collected, dried-powdered, passed through a sieve (number 80), and stored in desiccators for further use.

**Formulation of diclofenac sodium sustained release tablets:**

**Aim:** To prepare tablets of diclofenac sodium using natural polymers.

**Materials required:**

**Chemicals required:** Diclofenac sodium, flax seeds, hydroxy propyl methyl cellulose, xanthan gum, lactose monohydrate, polyethylene glycol, talc, magnesium stearate, isopropyl alcohol, acetone.

**Apparatus required:** Sieve 16, sieve 20, hot air oven, mortar, and pestle, measuring cylinder, muslin cloth.

**Procedure:** All the matrix tablets, each containing 100 mg of Diclofenac sodium, were prepared by wet granulation method, using Linum usitatissimum seed mucilage in different drug: mucilage ratios viz. 1:0.5, 1:1, 1:1.5. In the formulations prepared, lactose monohydrate was used as diluent. Seed mucilage was used as matrix-forming material, while polyethylene glycol was used as a binder. Tablets prepared with Hydroxypropylmethylcellulose (HPMC 50cps) and Xanthan gum as matrix forming material for the comparative study. Magnesium stearate 1% and talc 1 % were used as lubricant and glidant respectively. All ingredients were passed through a no.100 sieve, weighed, and blended. The tablets were prepared by wet granulation technique. Isopropyl alcohol was used as granulating fluid and it was added slowly to the power blend, and kneading was performed for few minutes until formation of wet mass. The wet mass was passed through a no.16 sieve and dried in a hot air oven for 3-5 hours. The dried granules were re-sieved through a no.20 sieve and thoroughly mixed with the lubricants and glidants. The lubricated granules were compressed by a single station tablet punching machine.

**Table1:** composition of diclofenac sodium sustained release tablets

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Ingredients** | **Quantity/ tablets(mg)** | | | | | | | | |
| **AF1** | **AF2** | **AF3** | **AF4** | **AF5** | **AF6** | **AF7** | **AF8** | **AF9** |
| Diclofenac sodium | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Flaxseed mucilage | 50 | 100 | 150 | - | - | - | - | - | - |
| HPMC |  |  | - | 50 | 100 | 150 | - | - | - |
| Xanthan gum | - | - | - | - | - | - | 50 | 100 | 150 |
| Lactose monohydrate | 234 | 184 | 134 | 234 | 184 | 134 | 234 | 184 | 134 |
| Polyethylene glycol | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 |
| Magnesium stearate | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| Talc | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| Isopropyl alcohol | Q. S | Q. S | Q. S | Q. S | Q. S | Q. S | Q. S | Q. S | Q. S |
| Total weight | 400 | 400 | 400 | 400 | 400 | 400 | 400 | 400 | 400 |
| Drug: polymer ratio | 1:0.5 | 1:1 | 1:1.5 | 1:0.5 | 1:1 | 1:0.5 | 1:0.5 | 1:1 | 1:0.5 |

**Standard calibration curve:**

**Aim:** To represent thestandard calibration curve of the diclofenac standard stock solution.

**Materials required:**

**Chemicals required:** Diclofenac sodium, distilled water.

**Apparatus required:** UV spectrophotometer

**Procedure:**

**Preparation of standard solution of diclofenac sodium:** 10 mg of Standard Diclofenac Sodium powder (99.54% pure) was dissolved in 5 ml of distilled water in a 10 ml volumetric flask then add volume up to mark with distilled water. Then 1 ml of this solution was diluted to 50 ml by adding distilled water. The concentration of this solution was 20 µg/ml.

**Preparation of calibration curve of diclofenac sodium:** 0.5 ml, 1 ml, 1.5 ml, 2.0 ml 2.5 ml, and 3.0 ml was taken from standard stock solution and diluted up to 50 ml by adding distilled water, the final concentration of these solution were 10 µg/ml, 20 µg/ml, 30 µg/ml,40 µg/ml and 50 µg/ml respectively. Absorbances of all solutions were measured at 275.8 nm. The observations were recorded and graphically presented.

**Evaluation parameters:**

**a) Precompression parameters of granules:**

**Aim:** To perform the precompression parameters for the prepared granules.

**Materials required:** funnel, measuring cylinder.

**Procedure:**

1. **Angle of repose:** The angle of repose was determined by the funnel method. A 10 g quantity of granules from formulation was weighed and allowed to flow from a funnel onto a flat horizontal surface so that it formed a cone. The height and the base of the cone formed were measured and recorded. This was repeated two more times and the mean value calculated. The same procedure was repeated for all the formulations. The angle of repose was calculated using equation:

**Tan θ = h/r**

Where,

h =height of the powder cone

r= radius of the powder cone.

**Table 2:** As perI.P. limits

|  |  |
| --- | --- |
| **Angle of repose** | **Flowability** |
| <25 | Excellent |
| 25-30 | Good |
| 30-40 | Passable |
| >40 | Very poor |

1. **Bulk Density:** Ten grams of granules was weighed from formulation AF1 and transferred into a 100 ml measuring cylinder. The volume occupied by the granules was recorded as the bulk volume. The procedure was repeated two more times and the mean bulk volume was determined. The procedure was repeated for all the formulations.

The bulk density was calculated using equation:

**Bulk density = weight of the powder / volume of the packing**

1. **Tapped density**: A 10 g quantity of granules was weighed from formulation AF1 and was transferred into a 100 ml measuring cylinder. The measuring cylinder was tapped 100 times and the new volume occupied by the granules was recorded as the tapped volume. The procedure was repeated two more times and the mean tapped density calculated. This was repeated for all formulations.

Tapped density was calculated using equation

**Tapped density = weight of the powder / tapped volume of the packing**

1. **Compressibility Index:** The compressibility index of the granules was determined by Carr’s compressibility index.

**Carr’s index (%) = [pt-po]/pt100**

Where,

Pt=tapped density and

Po=bulk density

**Table 3:** As perI.P. limits

|  |  |
| --- | --- |
| **Carr’s index** | **Properties** |
| 5-15 | Excellent |
| 12-16 | Good |
| 18-21 | Fair to passable |
| 23-35 | Poor |
| 33-38 | Very poor |
| >40 | Very very poor |

1. **Hausner’s ratio**: This was calculated using equation:

Hausner’s ratio = tapped density/bulk density

**Table 4:** As perI.P. limits

|  |  |
| --- | --- |
| **Hausner’s ratio** | **Flow character** |
| 1.00-1.11 | Excellent |
| 1.12.1.18 | Good |
| 1.19-1.25 | Fair |
| 1.26-1.34 | Passable |
| 1.35-1.45 | Poor |
| 1.46-1.59 | Very poor |
| >1.60 | Very very poor |

**b) Post compression parameters for tablets:**

**Aim:** To perform the post compression parameters for the prepared tablets.

**Materials required:** hardness tester, friabilator, disintegration test apparatus, dissolution test apparatus.

**Procedure:**

1. **Hardness:** Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm2. Three tablets were randomly picked, and hardness of the tablets were determined.
2. **Tablet Thickness:** The thickness of the tablets was determined by using vernier callipers. Five tablets were used, and average values were calculated.
3. **Weight Variation**: To study weight variation twenty tablets of the formulation were weighed using a digital balance and the test was performed according to the official method. The specification for weight variation of tablets as per USP. Twenty tablets were selected randomly and weighed individually to check for weight variation.

**Table5:** As per U.S.P. limits

|  |  |
| --- | --- |
| **Average weight** | **Percent difference** |
| 130mg or less | 10% |
| 130-324 | 7.5% |
| 324mg or more | 5% |

The tablets pass the USP test if no more than 2 tablets are out of percent limit and if no

tablet differs by more than twice the % limit.

1. **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 25 rpm for 4 minutes. The tablets were weighed again. The % friability was then calculated by:

**% Friability = Initial Weight – Final Weight / Initial Weight X 100**

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

1. **Disintegration Time**: Disintegration time test was carried out according to USP specification. 6 tablets were placed in a disintegration tester filled with distilled water at 37±0.20C. The tablets were considered completely disintegrated when all the particles passed through the wire mesh.
2. **In vitro dissolution test**: This test was carried out using the rotating basket method. A 900 ml quantity of phosphate buffer of pH 6.8 was used as the dissolution medium. One tablet of diclofenac sodium was weighed and placed in the basket of a single unit dissolution test apparatus. The basket was inserted into the dissolution chamber that was maintained at 37 ± 10c and rotated at a speed of 100 rpm. At predetermined time intervals of 1hr each from 1 to 6 hrs, 5 ml of the medium was withdrawn with a syringe and replaced with equal volume of fresh buffer medium. The samples withdrawn were filtered and analysed using the UV - VIS spectrophotometer at a wavelength of 276 nm.

**Table 6:** As per I.P. limits

|  |  |  |
| --- | --- | --- |
| **Stage** | **Number tested** | **Acceptance criteria** |
| S1 | 6 | Each unit is not less than Q +5% |
| S2 | 6 | Average of 12 units (S1+S2) is equal to or greater than Q and no unit is less than Q-15% |
| S3 | 12 | Average of 24 units (S1+S2 + S3) is equal to or greater than Q, not more than 2 units or less than Q-15%, and no unit is less than Q -25% |

**Results and discussion:**

**Calibration curve of diclofenac:**

**Table 7:** standard curve data

|  |  |
| --- | --- |
| **Concentration(mcg/ml)** | **Absorbance** |
| 10 | 0.112 |
| 20 | 0.223 |
| 30 | 0.325 |
| 40 | 0.441 |
| 50 | 0.535 |

**figure 1:** standard calibration curve of diclofenac sodium

**Table 8:** Preformulation parameters of granules

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Formulation code** | **Angle of repose** | **Bulk density**  **(gm/ml)** | **Tapped density**  **(gm/ml)** | **Carr’s index** | **Hausner’s ratio** |
| **AF1** | 29.41 | 0.73 | 0.85 | 15.52 | 1.171 |
| **AF2** | 27.31 | 0.76 | 0.87 | 14.34 | 1.166 |
| **AF3** | 27.22 | 0.75 | 0.86 | 14.23 | 1.206 |
| **AF4** | 26.83 | 0.73 | 0.83 | 13.62 | 1.186 |
| **AF5** | 28.04 | 0.74 | 0.86 | 15.25 | 1.183 |
| **AF6** | 25.75 | 0.77 | 0.86 | 11.87 | 1.198 |
| **AF7** | 25.96 | 0.79 | 0.88 | 16.56 | 1.216 |
| **AF8** | 27.30 | 0.78 | 0.89 | 17.45 | 1.175 |
| **AF9** | 28.58 | 0.75 | 0.90 | 16.04 | 1.186 |

**Table 9:** Physical properties of diclofenac sodium matrix tablets

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Formulation code** | **Average diameter(mm)** | **Average thickness(mm)** | **Friability**  **(%)** | **Hardness**  **(Kg/cm2)** |
| **AF1** | 11.56 | 3.33 | 0.323 | 10.01 |
| **AF2** | 11.36 | 3.70 | 0.318 | 9.06 |
| **AF3** | 11.63 | 3.66 | 0.511 | 7.53 |
| **AF4** | 11.55 | 3.74 | 0.832 | 10.32 |
| **AF5** | 11.61 | 3.65 | 0.227 | 9.43 |
| **AF6** | 11.54 | 3.52 | 0.505 | 7.65 |
| **AF7** | 11.63 | 3.61 | 0.816 | 9.03 |
| **AF8** | 11.55 | 3.55 | 0.345 | 8.45 |
| **AF9** | 11.58 | 3.22 | 0.513 | 7.88 |

**Results for evaluation parameters:**

**Table10:** Weight variation test

|  |  |  |
| --- | --- | --- |
| **Formulation code** | **Average weight of tablets** | **% Weight variation** |
| **AF1** | 398 | ±0.01 |
| **AF2** | 396 | ±0.02 |
| **AF3** | 396 | ±0.02 |
| **AF4** | 403 | ±0.02 |
| **AF5** | 398 | ±0.01 |
| **AF6** | 401 | ±0.01 |
| **AF7** | 403 | ±0.02 |
| **AF8** | 396 | ±0.02 |
| **AF9** | 401 | ±0.01 |

**Table 11:** Disintegration test

|  |  |
| --- | --- |
| **Formulation code** | **Disintegration time** |
| AF1 | 4min 40sec |
| AF2 | 5min |
| **AF3** | **5min 10sec** |
| AF4 | 4min 35 sec |
| AF5 | 4 min 40sec |
| AF6 | 4min 55 sec |
| AF7 | 4 min 20sec |
| AF8 | 4min 35sec |
| AF9 | 4 min 40sec |

**Table 12:** Dissolution data of diclofenac sodium tablets

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **S.no** | **Time (hrs)** | **% Cumulative drug release** | | | | | | | | | |
| **AF1** | **AF2** | **AF3** | **AF4** | **AF5** | **AF6** | **AF7** | **AF8** | **AF9** | **Marketed product** |
| **1.** | 1 | 32.26 | 37.40 | **34.46** | 38.15 | 32.20 | 38.36 | 36.85 | 38.23 | 37.10 | 36.14 |
| **2.** | 2 | 54.50 | 55.12 | **50.19** | 56.74 | 55.61 | 57.67 | 55.62 | 55.76 | 54.63 | 52.76 |
| **3.** | 3 | 62.14 | 59.17 | **64.21** | 69.85 | 64.27 | 60.23 | 64.36 | 62.92 | 70.55 | 66.22 |
| **4.** | 4 | 71.87 | 70.24 | **77.15** | 74.35 | 73.54 | 72.69 | 80.52 | 72.95 | 70.68 | 80.59 |
| **5.** | 5 | 80.49 | 83.69 | **87.99** | 80.68 | 82.21 | 81.58 | 79.14 | 85.73 | 84.66 | 89.95 |
| **6.** | 6 | 92.3 | 93.4 | **97.2** | 89.8 | 90.3 | 91.3 | 85.2 | 87.9 | 89.4 | 98.64 |

**Fig 2:** % drug release with flax seed polymer comparing with marketed formulation

**fig 3:** %drug release with HPMC polymer comparing with marketed formulation

**Fig 4:** %drug release with xanthan gum polymer comparing with marketed formulation

**REFERENCES:**

1. Kibbe AH, Editor, Handbook of pharmaceutical excipients, 3rd ed., London (UK), The Pharmaceutical Press, 2000.

2. Tripathy S, Pramod K, Banthia AK, Novel delivery system for aceclofenac, Scientific abstract, 56th Indian Pharmaceutical Congress, 2004, A71.

3. Srinivas K, Prakash K, Kiran HR, Prasad PM, Rao ME, Study of Ocimum basilicum and Plantago ovata as disintegrants in the formulation of dispersible tables, Indian J.Pharm.Sci., 65, 2003, 180.

4. Ernest Anderson and Harry J. Lowe, The Composition of Flaxseed Mucilage, http://www.jbc.org/. 5. Anoop Kumar Singh, Vipul Kumar Shingala, Panner Selvam R, Sivakumar T, Evaluation of Mangifera indica gum as tablet binder, International Journal of PharmTech Research, 2(3), 2010, 2098-2100.

6. Sumathi S and Ray Alok R, Release behaviour of drugs from tamarind seed polysaccharide tablets, J. Pharm. Sci., 5(1), 2002, 12-18.

7. Ghule B.V., Darwhekar G.D. Jain D.K. and Yeole P.G., Evaluation of binding properties of Eulophia campestris Wall. Mucilage, Ind. J.Pharm. Sci., 68(5), 2006, 566-569.

8. Indian pharmacopoeia 1996, vol. II, Govt. Of India, Ministry of Health & Family Welfare, The Controller of Publications, New Delhi, 554-555.

9. Indian pharmacopoeia 1996, vol. I, Govt. Of India, Ministry of Health & Family Welfare, The Controller of Publications, New Delhi 242-243.

10. Hamid A. Merchant, Once-daily tablet formulation and in vitro release evaluation of cefpodoxime using hydroxypropyl methylcellulose: A technical note, AAPS Pharm Sci Tech, 7 (3), 2006, 1-6.

11. Yeole PG, Galgatte UC, Babla IB, Nakhat PD, Design and evaluation of xanthan gum based sustained release matrix tablets of diclofenac sodium, Indian J.Pharm. Sci., 68(2), 2006, 185-189.

12. Talukdar M.M. and Kinget R., Swelling and drug release behaviour of Xanthan gum matrix tablets, Int J Pharm., 120, 1995, 63- 72.

13. Ansel HC and Loyyd VA. Pharmaceutical dosage forms and Drug Delivery System. Lippincott’s Williams and Wilking, Hong Kong. 1999; 8: 275-280.

14. Bonferoni MC and Rosi ST. Journal of Control Release.1993; 26: 119.

15. Sujja AJ, Munday DL, and Khan KA. Development and evaluation of a multiple-unit oral sustained release dosage form for S(+)- ibuprofen: preparation and release kinetics.Int. J. Pharm. 1999; 193(1): 73-84.

16. Jain NK, Kulkarni K and Talwar N. Controlled release tablet formulation of isoniazid. Pharmazie. 1992; 47: 277.

17. Altaf S. and Jones DB. Controlled release matrix tablets of isoniazid, diltiazem and nafronyl oxalate. Pharm. Res.1998; 15: 1196. G.N.K. Ganesh et al, /J. Pharm. Sci. & Res. Vol.2 18. 2010, 360-368 Ebihara et al., Controlled release formulations to increase the bio adhesive properties, Drug Res. 1983; 33: 163.

19. Indian Pharmacopoeia. Ministry of health. The controller of publications, New Delhi. 1996; 4ed.; 735.

20. Indian Pharmacopoeia. Ministry of health. The controller of publications, New Delhi. 1996; 4ed; 432. [9] Lachman L, Liberman HA and Kanig JL. The Theory and Practice of Industrial Pharmacy. Varghese Publishing House, Mumbai, 1991; 3rd Edn; 88.

21. Akbari J, Nokhodchi A and Farid D. Development and evaluation of buccoadhesive propranolol hydrochloride tablet formulations: effect of fillers. Int. J. Pharm. 2004; 59(2): 155. 22. Nayak AK (2010) Thermodynamic study of the diclofenac sodium solubility in various oils. Chemistry 19: 121-128.

23. Timmakondu S, Prabu SL, Satyam T (2011) In-vitro studies of diclofenac sodium controlled-release dosage from biopolymeric hydrophilic matrices. Ars Pharm 52: 20-24.

24. Giri TK, Parveen N, Thakur D, Tripathi DK (2012) In vitro Evaluation of Commercially Available Enteric Coated Tablet Containing Diclofenac Sodium. IJRPBS 3: 875-881.

25. UI-Hassan SS, Yunus SH, Latif A (2010) Study and Improvement of Methods for the Determination of Diclofenac Sodium in Pharmaceutical Preparations. Pak J Pharm 23: 7-10.