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Original Research Article

Formulation and Evaluation of Swellable Matrix Tablet Using Emerging Excipient *Hibiscus Esculentus*

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ABSTRACT

The present study was undertaken with an objective to expound the swelling ability of Hibiscus esculentus Linn (HEP) powder and its capability to sustain the release of drug. The Okra mucilage was prepared using water extraction method. The physio chemical properties of Okra powder were studied. Ibuprofen was selected as a model drug to observe the sustain character of Okra. FTIR of Okra shows that it has same IR spectra like other polymer such as HPMC. Swellable matrix tablet was prepared by direct compression method using Ibuprofen, Okra Power, HPMC, lactose, magnesium sterate, talc. Combination of Okra and HPMC in the ratio of 25:25 was used in formulation F4 and it was found to be the best one. The formulations were optimized on the basis of acceptable weight variation, thickness, hardness, % friability, % drug content and in vitro drug release. The in vitro release studies were performed using USP type II apparatus using 7.2 pH phosphate buffers as dissolution medium, showed that optimized formulation F4 was found to sustain the release of Ibuprofen over a period of 12 hr.

***Key Words*:** *Hibiscus esculentus* Linn, sustain release, HPMC, in vitro release studies

INTRODUCTION

A major challenge for the pharmaceutical industry in drug development is to produce safe and efficient drugs, therefore properties of drugs and the way in which they are delivered must be optimized. [1] Traditional drug delivery system has been characterized by immediate release and repeated dosing of the drug which might lead to the risk of dose fluctuation, this arises the need of a formulation with control release that maintain a near-constant or uniform blood level. The desire to maintain a near-constant or uniform blood level of a drug often translates into better patient compliance, as well as enhanced clinical efficacy of the drug for its intended use.

Drawbacks of Conventional Dosage Forms: -

- Poor patient compliance.
- Increased chances of missing the dose of a drug.
- The unavoidable fluctuations of drug concentration.
- Difficult to attain plasma concentration time profile steady-state condition.
- The fluctuations in drug levels of a drug with small Therapeutic Index (TI) may lead to precipitation of adverse effects whenever over medication occur. [2]

These drawbacks are overcome by formulating controlled release dosage form which leads to fruitful changes in medical field. Amazing feature of controlled release

formulation is that they release one or more drugs continuously in predetermined pattern for a fixed period of time. More concentrated studies are paid on development of oral controlled release drug delivery systems due to flexibility in designing of dosage form. The main challenges to oral drug delivery systems are to deliver a drug at therapeutically effective rate to desirable site, modulation of GI transit time and minimization of first pass elimination. These challenges can solved by control release dosage form which provides better maintenance of optimal and effective drug level for prolonged duration with less dosing frequency and side effects.

There are many factors that need to be taken into consideration when designing such formulations for obtaining above mentioned desirable effects. Some of these are as follows:

- Different drug solubility's need to be consider because highly soluble drugs will dissolve immediately after administration. Reduced drug solubility increases the tendency of the tablet to erode due to particle displacement.
- The drug should have a short half-life. If a drug has a long half-life then there is a risk of accumulation as it will be eliminated at a slower rate compared to its absorption.
- A drug that is tested in-vitro needs to be able to provide similar release characteristics once administered and is under pathophysiological or in-vivo conditions. A direct correlation of in-vitro data with in-vivo release is not possible without thorough and careful analysis. Some factors need to be considered when designing tablets for extended release which varies its concentration in different part of gastrointestinal tract.
- The dissolution characteristics should allow for drug to be released in a controlled manner, highlighting the importance for the correct selection of polymers according to their physical, mechanical and pharmacokinetic properties. [1]

Different Types of Sustained Release

There are several types of sustained release systems that are designed and categorized according to the mechanism they employ. [2]

- Dissolution controlled release
  - Encapsulated dissolution system
  - Matrix dissolution system
- Diffusion controlled system;
  - Reservoir diffusion system
  - Matrix diffusion system
  - Reservoir diffusion system
- Dissolution & diffusion controlled release
- Ion exchange resins controlled release system
- Osmotically controlled release system

Matrix Dissolution System

- Rigid Matrix Diffusion: Materials used are insoluble plastics such as PVP & fatty acids.
- Swellable Matrix Diffusion: it is also called as Glassy hydro gels and popular for sustaining the release of highly water soluble drugs. Materials used are hydrophilic gums. Examples:

Natural- Guar gum, Tragacanth.

Semi synthetic -HPMC, CMC, Xanthum gum.

Synthetic -Polyacrilamides.

These systems involve drug to be encapsulated or dispersed in a matrix. These systems can be employed by forming hydrophobic matrices and/or hydrophilic matrices to allow for control or prediction of drug release. They can be divided into soluble/hydrophilic matrix systems which swell on hydration and dissolve to release drug and insoluble/hydrophobic matrix systems which release drug after being dissolved by a solvent.

Hydrophobic matrix systems are formulated by waxes mainly and can be suitable for drugs which have a high solubility. Wax based matrices have been investigated to ascertain the factors that

would affect the release of drug. Drug release has been successfully modulated in hydrophobic matrices. Even though the hydrophobic matrix are able to modulate drug release, the processes that had to be carried out such as hot fusion and thermal treatment highlighted the length of the process that would be required to form such tablets. This can potentially be a deterrent for manufacturing companies who would prefer a more economical method of producing sustained release formulations. [14]

Hydrophilic matrix systems tend to be more popular in tablet manufacture for controlled release drug delivery systems due to their low manufacturing cost. On contact with water a hydrophilic matrix increases in size due to the entry of the solvent. This then allows the polymer to swell up forming a barrier to drug release. The drug particles would then move through this gel layer via diffusion or erosion of the gel eventually allowing drug to be released. There has been a lot of research into the mechanisms of drug release from hydrophilic matrices and the critical factors that influence the release rate. These swellable matrices have more than one 'front' as a part of its release mechanism. This has been shown in figure 1. [1]

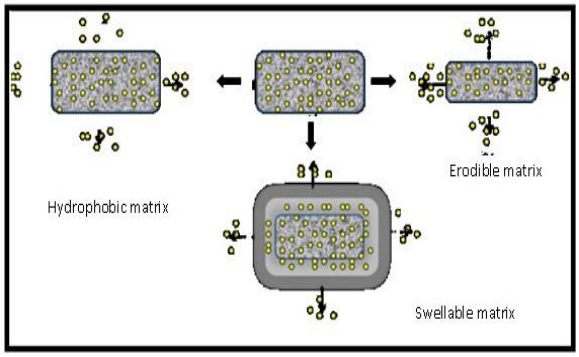

Figure 1: Schematic representation of drug release from different types of matrix tablets. [1]

Factors Affecting Drug Release from Matrix Tablet

- Swelling characteristics of polymers.
- Polymer erosion.
- Drug loading.
- Drug solubility.

Advantages of Matrix Tablets

- Maintains therapeutic concentrations over prolonged periods hence avoid the high blood concentration.
- Reduction in toxicity by slowing drug absorption.
- Minimize the local and systemic side effects.
- Improvement in treatment efficacy by better drug utilization.
- Minimize drug accumulation with chronic dosing.
- Can be made to release high molecular weight compounds.
- Increase the stability by protecting the drug from hydrolysis or other derivative changes in GIT.
- Reduction in health care cost and improved patient compliance.
- Improvement of the ability to provide special effects. Ex: Morning relief of arthritis through bed time dosing.

1.3.4. Disadvantages of Matrix Tablets.

- The remaining matrix must be removed after the drug has been released.
- Greater dependence on GI residence time of dosage form.
- Increased potential for first-pass metabolism.
- Delay in onset of drug action.
- Release rates are affected by food and the rate transit through the gut. [3]

The use of natural gums for pharmaceutical application is attractive because they are economical, readily available, non toxic, bio compatible. Lots of natural polymers from various plant sources have been successfully used and others are being investigated as excipient in design of dosage form for effective sustained release drug delivery. Tamarind gum, Okra gum, Hakea gum, Karaya gum, Fenugreek mucilage are some Plant sources for synthesis of polymer. 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. These have also been utilized as viscosity enhancers, stabilisers, disintegrants, solubilisers, emulsifiers, suspending agents, gelling agents and bioadhesives, binders.

Aim of the present study is to formulate and evaluate swellable matrix tablet using an excipient which is extracted from pods of Okra.

The brief plan of work is to extract Okra gum mucilage and use as an excipient. For the study of effectiveness of its ability to control drug release, non steroidal anti inflammatory drug Ibuprofen is choose as a model drug.

MATERIALS & METHODS

The plant materials required for the study was collected from local market.

Extraction of pods of Hibiscus esculentus

1 kg of unripe and tender Okra fruits (pods) was obtained from the local market. The seeds were removed as they do not contain any mucilage. The fruits were washed and sliced thinly with a knife. The sliced mass was soaked in distilled water overnight to extract out the mucilage. After soaking, a white muslin cloth was used to filter out the viscous gum extract (mucilage). Acetone was added to precipitate the gum at a ratio of 3 parts of acetone to 1 part of the gum extract. [4] Gum extract was dried on oven at 60^0C for 72 hrs. Size was reduced and stored in a desiccator.

Preformulation Studies

Preformulation testing is the first step in the rational development of a dosage form of the drug substance. The overall objective of the study is to generate information that is useful in developing stable dosage forms.

Analysis of Ibuprofen

FT-IR Spectroscopy of ibuprofen

The FT-IR spectrum of the obtained sample of drug and polymer were compared with the standard functional group frequencies of Ibuprofen, Okra gum mucilage, HPMC K100M, respectively.

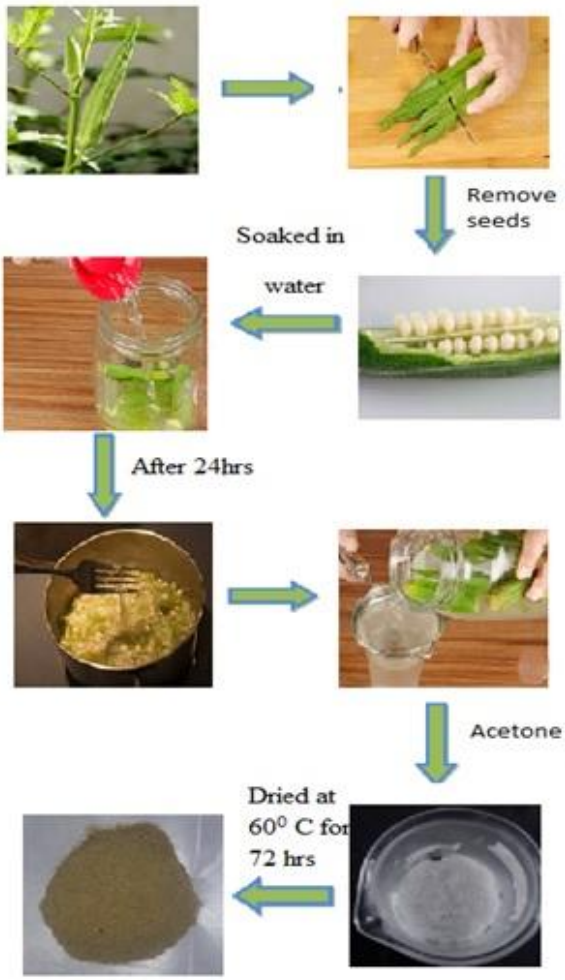

Figure 2: Steps involved in the extraction of Okra gum powder

Preparation of Calibration Curve of Ibuprofen

Preparation of stock solution (100µg/ml);

A weight of accurately 10mg of Ibuprofen was taken and dissolved, then made up to 100ml with pH 7.2 phosphate buffer.

Preparation of working standard solution

From the stock solution different volumes of 1ml, 2ml, 4ml, 6ml, 8ml, 10ml and 12ml were taken and diluted up to 100ml in a volumetric flask with pH 7.2 phosphate buffer to give the concentrations of 1µg/ml, 2µg/ml, 3µg/ml, 4µg/ml, 5µg/ml, 6µg/ml, 8µg/ml, 10µg/ml and 12µg/ml respectively. The absorbance was measured at 221nm in UV-Visible spectrophotometer against phosphate buffer pH 7.2 as blank

and standard curve was plotted taking concentration Vs absorbance.

Physiochemical Evaluation of Okra Gum Powder

Organoleptic properties of the Okra gum powder

The physical appearance such as colour and odour of excipient was observed.

Determination of melting point

Melting point of Okra gum powder was determined by capillary method.

Solubility

Solubility test of Okra gum powder was done by adding 1g of gum powder to 10ml of solvent (Distilled water, acetone, Phosphate buffer ph 7.2) in a 25ml stoppered standard flask with vigorous shaking.

Loss on drying

The loss on drying test is designed to measure the amount of water and volatile matters in a sample when the sample is dried under specified conditions.

Loss on drying = [(W1 – W2) / W1] x 100

Where;

W1=initial weight

W2=final weight

pH determination [4]

1%w/v dispersion of the sample in water was stirred consistently for 5 minutes and pH was determined using a pH meter.

Swelling characteristics [5]

Swelling characteristics of mucilages were tested in distilled water, and phosphate buffer (pH 7.2). The Swelling index is the volume in ml occupied by part (1g) of the substance. The Swelling index of the mucilage powder was determined by according to British Pharmacopoeia method. The test was performed by taking 1g of the mucilage powder in a 100ml ground glass stoppered graduated cylinder. To this 100ml of distilled water, phosphate buffer (pH 7.2) was added and this was shaken vigorously every 10min and then allowed to stand for 24 hrs. The volume occupied by the mucilage powder was measured.

The swelling index of mucilages powder was calculated according to the following equation

SI = (V2-V1) /V1

Where,

V1 is volume occupied by the mucilage prior to hydration

V2 is volume occupied by the mucilage after hydration.

Pre-Formulation Studies of Powder Blend

- Angle of repose
- Bulk density
- Tapped density
- Compressibility index or Carr's index (CI)
- Hausner ratio

Formulation of Ibuprofen Tablet

Different tablet batch formulations (F1-F10) were prepared by direct compression method. Pure drug and polymers (okra, HPMC K 100) were mixed well for 10min in motor and pestel. To this blend lactose (diluents) was added and mixed for 5min.

Table: 1: Formulation trials of Ibuprofen 250 mg

INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Ibuprofen(mg)	100	100	100	100	100	100	100	100	100	100
Okra gum (mg)	x	x	40	25	50	75	20	40	35	x
HPMC K 100 M (mg)	75	50	40	25	x	x	40	20	25	25
Lactose(mg)	74.92	99.92	69.92	99.92	99.92	74.92	89.92	89.92	89.92	124.92
Talc (mg)	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Magnesium sterate(mg)	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Total weight of tablet(mg)	250	250	250	250	250	250	250	250	250	250

This powder blend was lubricated with sufficient amount of Magnesium sterate and Talc and then directly compressed into tablets using a single punch rotary tablet punching machine.

Evaluation of Prepared Formulation

Organoleptic properties: The physical appearance such as colour and odour of tablet was observed.

Thickness: The thickness of the matrix tablets was determined using vernier calliper and the results were expressed as mean values of 3 determinations, with standard deviations.

Weight uniformity test [6,7]: Twenty tablets from each batch were weighed using an electronic balance together and individually, and calculated the average weight and percentage deviation.

Table 2: Weight variation specification as per IP [13]

Average weight of tablet	% deviation
80mg or less	±10
More than 80mg but less than 250mg	±7.5
250mg or more	±5

Hardness measurement: [8,9] For each formulation, the hardness of 5 tablets (according to IP) was determined using a hardness tester (Pfizer). Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage, transportation and handling before usage depends on its hardness.

The force required to break the tablets is measured in kilograms and a crushing strength of 4kg is usually considered to be minimum for satisfactory tablets. The mean crushing strength (hardness) was determined, and the data are presented in the. Table 18

Friability: Ten tablets (according to IP) were randomly selected from each batch and weighed. The tablets were set to rotate for 100 revolutions in a friabilator (Roche Friabilator, DBK instruments). Tablets were dusted and reweighed. Compressed tablets should not lose more than 1% of their weight. The friability was calculated according to the formula:

% Friability= [(Initial weight−Final weight)/Initial weight] ×100

Swelling Index of Tablet [10]

The swelling of tablet involves the absorption of a liquid resulting in an increase in weight and volume. Liquid uptake by the polymers results to saturation of capillary spaces within the polymer chain or hydration of macromolecule. To determine the extent of matrix swelling, tablets from each batch were weighed and placed in a petri-dish containing 25ml of phosphate buffer 7.2. After each 1 hrs interval the tablets were removed from media, excess of media was wiped off by using filter paper and weighed again up to 12hr. The swelling index was calculated using following formula.

Swelling Index S.I. = (Wt-W0)/W0)*100

Drug content [11]

Accurately weighed the quantity of the tablet powder equivalent to 10mg of the drug was transferred to 100ml volumetric flask. 50ml of buffer solution of pH-7.2 was added. Mix with the aid of ultrasound for 10min, and then the volume was made up to 100ml with the same buffer solution, 2 ml of the filtrate was diluted to 100ml with same buffer solution and examined under U.V Spectrophotometer at 221nm.

In vitro release studies [12]

The release rate of Ibuprofen from tablets was determined using United States Pharmacopeia (USP) Dissolution Testing Apparatus 2 (paddle method). The dissolution test was performed using 900ml of 7.2 pH phosphate buffer, at 37 ± 0.5 ^{0}C and 50rpm. A sample (1ml) of the solution was withdrawn from the dissolution apparatus hourly and the samples were replaced with fresh dissolution medium. The samples were diluted to a suitable concentration with 7.2 pH phosphate buffer. Absorbance of these solutions was measured at 221nm using a Thermospectronic-1 UV/V is double-beam spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from a standard curve. The results are shown in Table no 21,22.

Dissolution test parameters

Dissolution test apparatus: USP XXII type II (paddle)
Dissolution medium: phosphate buffer 7.2
Temperature of medium: 37 ± 0.5°C
Speed of rotating paddle: 50 rpm
Sampling volume: 1 ml

RESULT

Collection and Extraction Of Plant Materials

Okra pods are extracted and approximately 5g was obtained from 1kg of pods

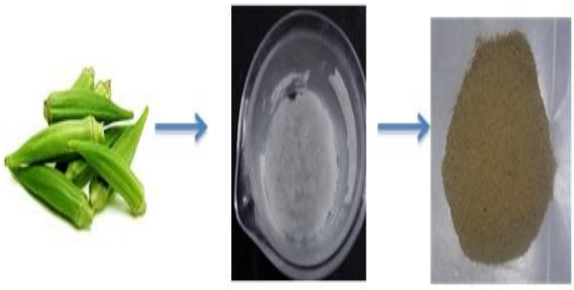

Figure 3: Shows different steps of extraction of okra gum powder

Preformulation Studies

Organoleptic properties of the drug

Table 3: Organoleptic properties of drug

SI. No:	Tests	Specification(BP)	Observation
1	Character	white or almost white, crystalline powder	White coloured crystalline powder
2	Colour	White	White
3	Taste	Tasteless	Tasteless

Determination of melting point

Table 4: Melting point of Ibuprofen

Property	Specification(BP)	Observation
Melting point	75-780C	750C

Solubility

Table 5: Solubility of drug

Sl.No	Solvent	Solubility
1	Distilled water	Insoluble
2	Acetone	Freely soluble
3	Phosphate buffer 7.2	Soluble

Solubility of Ibuprofen in various solvents such as distilled water, acetone and phosphate buffer 7.2 were studied and found that it is freely soluble in acetone while it is slightly soluble in acetone, soluble in phosphate buffer 7.2 and insoluble in distilled water.

FT-IR Spectroscopy of ibuprofen

The FT-IR spectrum of Ibuprofen is shown in figure 4, which complies with standard functional group frequencies.

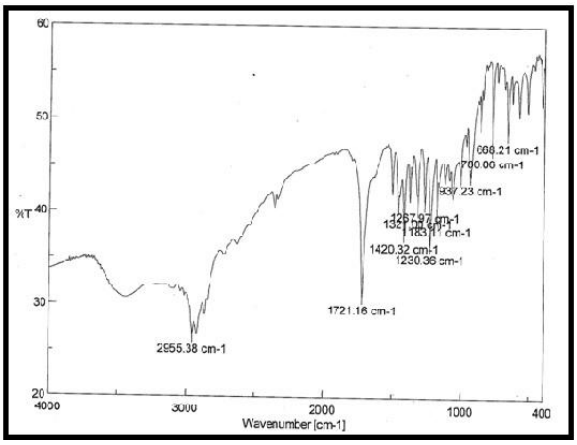

Figure4: FT-IR spectrum of Ibuprofen

Table 6: IR frequencies of Ibuprofen

Functional group	Characteristic wave number	Ibuprofen observed wave number
COOH	1725-1700	1721.16
Methyl C-H stretch	2970-2950	2955.38
Skeletal C-C vibration	1300-700	780.6
Vinyl C-H in plane	1420-1410	1420.06

The peaks analyzed in the Table 7 indicate the most characteristic frequencies of functional group of Ibuprofen which are COOH, C-H, C-C, etc were confirmed and comply with the reported frequencies.

Compatibility between drug and polymer

The FT-IR spectrum of Ibuprofen is shown in figure 4 and combination of Ibuprofen with excipients are shown in figure 5.

The compatibility between drug-polymer was carried out using FT-IR peak matching method. All major peaks present in the spectrum of pure drug were observed in the spectrum of drug-polymer mixture. This suggests the absence of any chemical interaction and it concluded that there was

no incompatibility between drug and polymers.

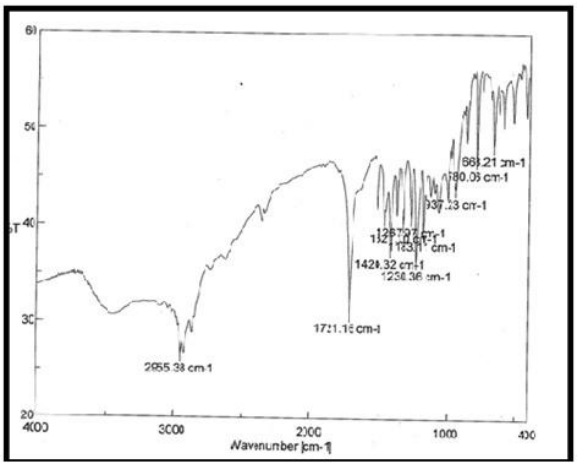

Figure 5: FT-IR spectrum of physical mixture of Ibuprofen with polymers

Table 8: IR frequencies of Ibuprofen with polymers

Functional group	Characteristic wave number	Ibuprofen observed wave number	Ibuprofen-polymer mixture (wave number)
COOH	1725-1700	1721.16	1721.16
Methyl C-H stretch	2970-2950	2955.38	2955.38
Aromatic C-H out-of-plane bend	900–670	780.6	780.6
Vinyl C-H in plane	1420-1410	1420.06	1420.06

Preparation of Calibration Curve of Ibuprofen

Preparation of phosphate buffer solution pH 7.2

173.5ml of 0.2N NaOH and 250ml of 0.2 M potassium dihydrogen phosphate was prepared and mix together and finally makeup to produce 1000ml of buffer solution.

Preparation of 0.2 N NaOH

Dissolved 8g NaOH pellets in 1000ml standard flask and make up with distilled water.

Preparation of 0.2 M KH_2PO_4

Dissolved 27.22g of KH_2PO_4 in 1000ml standard flask and make up with distilled water**.** Table shows the absorbance of standard solution containing 1-12µg/ml of drug in phosphate buffer pH7.2.

Table 9: Standard calibration table for Ibuprofen in phosphate buffer pH 7.2 at 221 nm

Sl.No	Concentration (µg/ml)	Absorbance(at 220 nm)
1	1	0.098
2	2	0.139
3	4	0.206
4	6	0.589
5	8	0.795
6	10	0.889
7	12	0.992

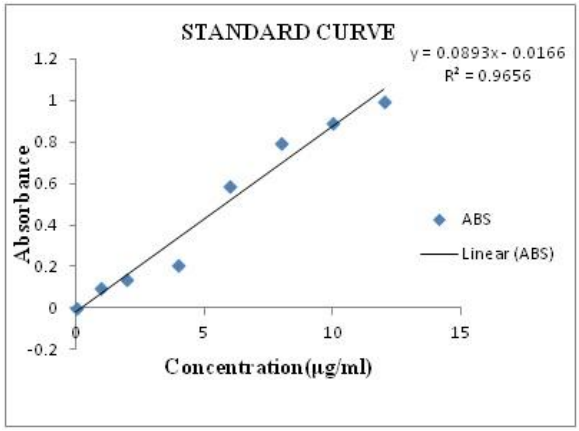

Figure6: Standard graph of Ibuprofen in phosphate buffer 7.2

Plotted calibration curve was found to be straight line with slope of 0.0893. Calibration curve could be used for finding unknown concentration of drug, for the further studies of drug content, release profiling etc.

Physiochemical Evaluation of Okra Gum Powder

Organoleptic properties of the Okra gum powder

Table.10: Organoleptic properties of Okra gum powder

Sl.No	Tests	Observation
1	Character	Coloured powder
2	Colour	Slightly brown
3	Taste	Sour

Determination of melting point

Table 11: Melting point of Okra gum powder

Property	Observation
Melting point	60.2^0C

Solubility

Table 12: Solubility of Okra gum

Sl. No	Solvent	Solubility
1	Cold water	Swell to form gel
2	Hot water	Soluble
3	Acetone	Insoluble
4	Phosphate buffer 7.2	Insoluble

Solubility of Okra gum powder in various solvents such as cold water, hot and Phosphate buffer 7.2 were studied and found that it is freely soluble in hot water, in cold water it swell to form gel but insoluble both in acetone and Phosphate buffer.

Loss on drying

Table13: Loss on drying of Okra powder

Property	Observtion
Loss on drying	0.33% w/w

The value obtained in loss on drying was less, it suggests that it contain less moisture content so it is found to be stable.

pH Determination

Table 14: pH of Okra powder

Property	Observation
pH	6.92

pH of Okra powder was found to be approximately neutral so it is suitable for uncoated tablet due to its less irritancy.

Swelling Characteristics of Okra powder

Table 15: Swelling Characteristics of Okra power

Medium	V1 (volume occupied before hydration)	V2(volume occupied after hydration)	Swelling index
Distilled water	2.3	10	3.347
Phosphate buffer pH 7.2	2.2	10.1	3.59

Swelling index of Okra powder was observed both in water and phosphate buffer 7.2 and it was found that swelling of Okra powder was high at phosphate buffer pH 7.2 than distilled water.

MICROMERITIC PROPERTIES OF FORMULATION BLENDS

Table 16: Micromeritic properties of formulation blends

Formulation	Angle of repose	Bulk density	Tapped density	Carr's index	Hausner's ratio
F1	32+0.23	0.54+ 0.00	0.62+ 0.001	12.16+ 0.170	1.14+ 0.002
F2	34.28 +0.45	0.51+ 0.001	0.63+ 0.001	19.56+ 0.055	1.24+ 0.001
F3	30.96 +0.11	0.54+ 0.002	0.62+ 0.0030	12.84+ 0.586	1.15+ 0.008
F4	29.05 +0.32	0.54+ 0.001	0.60+ 0.001	9.82+ 0.291	1.11+ 0.004
F5	36.86 +0.27	0.52+ 0.001	0.68+ 0.002	22.94+ 0.313	1.30+ 0.005
F6	32 +0.02	0.55+ 0.001	0.69+ 0.013	20+ 1.478	1.25+ 0.022
F7	33.11 +0.03	0.53+ 0.001	0.69+ 0.011	22.63+ 1.467	1.29+ 0.023
F8	29.05 +0.46	0.054+ 0.001	0.71+ 0.032	24.86+ 4.237	1.33+ 0.062
F9	36.86 +0.29	0.50+ 0.002	0.59+ 0.012	16.10+ 1.27	1.19+ 0.019
F10	31 +0.02	0.54+ 0.00	0.63+ 0.001	13.85+ 0.14	1.16+ 0.002

Irregular flow of powders from the hopper produces tablets with non uniform weights. As a result content uniformity and dose precision cannot be achieved in production of tablets and capsules. Flow property of powder can be determined by using angle of repose. The angle of repose of the prepared powder blends ranges from 29.05^0 to 36.86^0, indicates good and passable flowability.

The bulk density of a powder depends primarily on particle size distribution, particle shape and the tendency of the particles to adhere to one another. The blends of different formulations were evaluated for bulk density. The bulk density of the prepared powder blends ranges from 0.50 to 0.55g/cc.

The blends of different formulations were evaluated for tapped density. The tapped density of the prepared powder blends ranges from 0.59 to 0.69g/cc.

The powder blends were evaluated for their compression properties. The compressibility index lies within the range of 9.82 to 24.86%, indicates good and passable compression properties.

The Hausner's ratio of the prepared powder blends ranges from 1. 11 to 1.33. Lower Hausner's ratio less than 1.25 shows better flow properties.

Based on above observation it showed that formulation F4 comply with all the requirements of powder flow property and shows values within range.

Evaluation of Tablet

Organoleptic evaluation

All the prepared formulations showed specific colour without specific odour.

Table 17: Organoleptic properties of Formulations F1-F10

Formulation code	Colour	Odour
F1	White	None
F2	White	None
F3	Light brown	None
F4	**Light brown**	**None**
F5	Light brown	None
F6	Light brown	None
F7	Light brown	None
F8	Light brown	None
F9	Light brown	None
F10	white	None

Post compression parameters:

Table 18: Post compression parameters

Formulation	Thickness (mm)	Average weight of tablet	Hardness (mm)	%friability
F1	5.30	256	8.20	0.409
F2	5.00	253	4.70	0.784
F3	5.10	253	7.73	0.962
F4	5.00	250	5.63	0.534
F5	5.10	252	6.70	0.859
F6	4.70	249	5.40	0.800
F7	4.70	248	6.40	0.401
F8	5.00	245	6.80	0.842
F9	4.90	246	5.73	0.803
F10	4.80	249	4.90	0.801

Average weight Of 20 tablets were evaluated. The values are almost uniform and closest to mean value and were within specification. Hardness, friability, thickness of tablets was evaluated and hardness ranged from 4.70 -8.20 mm and friability ranged from 0.409-0.962, so the tablets of all formulations are within the specific limit.

Swelling Index of Tablet

Table 19: Swelling index of tablet

TIME	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	153.85	200.00	176.92	70.83	x	x	119.23	58.33	139.13	156
2	157.69	204.17	176.92	87.50	x	x	123.08	70.83	139.13	164
3	173.08	208.33	180.77	87.50	x	x	123.08	83.33	139.13	176
4	184.62	220.83	188.46	95.83	x	x	126.92	116.67	156.52	176
5	196.15	229.17	188.46	112.50	x	x	130.77	120.83	156.52	192
6	203.85	229.17	188.46	129.17	x	x	130.77	129.17	156.52	208
7	207.69	233.33	188.46	137.50	x	x	142.31	154.17	169.57	216
8	207.69	233.33	203.85	145.83	x	x	142.31	162.50	173.91	220
9	211.54	237.50	203.85	170.83	x	x	153.85	187.50	200.00	224
10	211.54	241.67	211.54	187.50	x	x	153.85	212.50	217.39	224
11	215.38	245.83	215.38	200.00	x	x	157.69	233.33	239.13	224
12	215.38	258.33	250.00	259.17	x	x	161.54	238.00	255.22	228

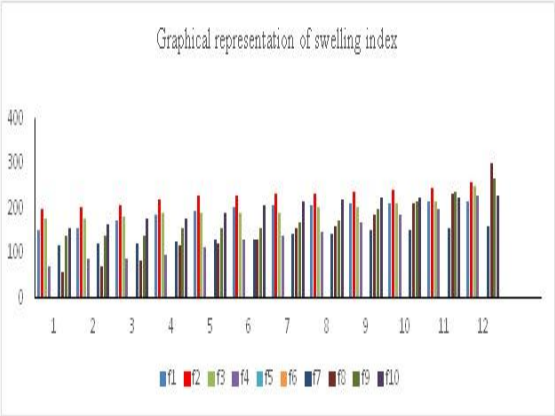

Figure 7: Graphical representation of swelling index

Swelling index of F4 formulation was found to be high. Formulation F5 and F6 doesn't show any swelling character due to the lack of HPMC. As swelling index increases drug retardation decreases. So formulation F4 had highest sustaining capability.

Drug content

Drug content estimation of all formulations was carried out by using UV spectrophotometer at 221nm and was found

to be in the range of 95.29 – 102.23% which is in the range specified in IP (95-105). The maximum % drug content was found to be 97.33 % in F1.

Table 20: Drug content

Formulation	%Drug content
F1	96.04
F2	101.23
F3	97.89
F4	102.23
F5	96.20
F6	96.15
F7	95.29
F8	95.66
F9	103.69
F10	97.48

In vitro release studies

In-vitro dissolution studies of all formulations of Ibuprofen were carried out in dissolution test apparatus using phosphate buffer pH 7.2 as the dissolution medium for 12 hr. Percentage cumulative drug release at each time interval was shown in the table and the data represented graphically

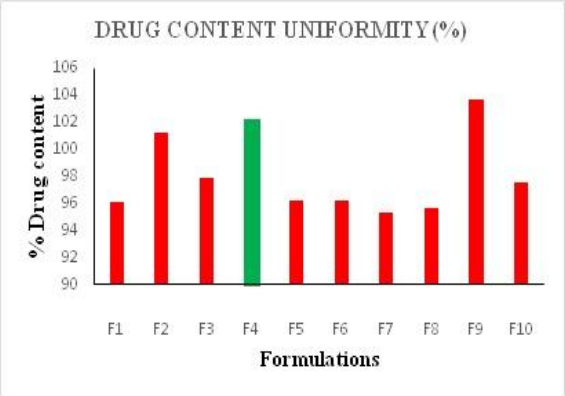

Figure 8: Graphical representation of drug content

Table 21: Percentage cumulative drug release of formulation (F1-F5).

Time	F1	F2	F3	F4	F5
1	15.44±0.41	45.55±1.0	15.66±0.32	**32.9±0.54**	76.37±1.22
2	17.45±0.64	51.45±1.42	18.40±0.31	**43.99±0.51**	75.35±0.12
3	17.90±0.65	54.29±0.97	20.34±0.22	**52.36±0.50**	76.87±0.41
4	18.81±0.69	55.82±0.97	21.15±0.46	**59.12±0.22**	78.60±0.58
5	21.25±0.22	57.45±1.15	23.59±0.57	**64.57±0.12**	78.90±0.31
6	22.37±0.42	57.55±0.06	26.64±0.81	**68.61±0.34**	79.62±0.22
7	24.72±0.90	59.68±1.5	29.68±0.54	**73.96±0.41**	82.47±1.15
8	26.65±0.30	61.21±0.47	32.64±0.10	**80.31±0.61**	87.25±1.10
9	29.16±0.26	63.36±0.55	37.11±0.80	**85.96±0.45**	93.13±2.25
10	32.79±0.44	69.21±0.32	41.73±0.31	**89.90±0.86**	99.67±1.79
11	34.91±0.42	72.95±0.63	46.10±0.02	**94.03±0.55**	99.79±0.47
12	40.25±0.60	76.28±0.67	49.22±0.71	**97.36±0.93**	99.90±0.51

Table 22: Percentage cumulative drug release of formulation (F6-F10).

Time	F6	F7	F8	F9	F10
1	66.30+0.15	23.71+0.14	37.53+0.01	27.34+0.14	38.84+0.70
2	66.81+0.40	28.76+0.63	44.60+0.42	31.78+0.58	40.86+0.54
3	70.67+0.36	33.80+0.63	54.38+0.75	35.21+0.31	41.06+0.52
4	70.67+0.13	40.46+0.85	63.87+0.58	40.16+0.37	44.29+0.23
5	70.73+0.07	45.60+0.83	64.67+0.76	42.98+0.92	48.73+0.01
6	70.77+0.12	48.83+0.85	64.88+0.79	46.11+0.6	50.85+0.03
7	71.78+0.20	54.89+0.59	65.28+0.77	47.93+0.68	54.89+0.47
8	71.79+0.37	58.32+0.26	66.79+0.49	52.06+0.27	60.34+0.67
9	74.22+0.69	61.75+0.49	67.40+0.66	55.29+0.62	62.66+0.41
10	74.28+0.79	65.56+0.04	67.60+0.98	57.61+0.64	64.78+0.87
11	76.00+0.92	72.14+0.55	68.81+0.83	63.36+0.40	69.92+0.59
12	79.67+0.18	74.31+0.96	71.43+0.26	71.84+0.07	72.14+0.98

Formulation F1, F3 shows slow release of drug, only 40% of drug was released in 12 hrs. Formulations F2, F6 and F10 had a high initial release but before that drug release were reduced. Formulations F4 shows sustained release over 12 hrs. Formulations F7 and F8 shows slow release as compared with other formulations. In F1, F2 HPMC was used as polymer and in F5&F6 okra was used. In F4 25% of okra and 25% of HPMC was used and this formulation shows sustained release of drug. This concluded that combination of HPMC with Okra in 25:25 makes the formulation good to sustain the release.

Kinetics of in vitro drug release.

The results obtained of in vitro release studies were attempted to fit into various mathematical models.

The in vitro drug release data was subjected to goodness of fit by linear regression analysis, according to zero order, first order kinetic equation, Higuchi and Korsmeyer models to ascertain the mechanism of drug release.

When the regression coefficient 'R^2' values of zero order and first order plots were compared, it was observed that the 'R^2' values of zero order was higher than that of first order plots which indicate that the drug release from the formulations is more likely to follow zero order kinetics .

Based on the values of regression coefficient, it was concluded that the formulation F4 strictly follows zero order kinetics compared to other formulation from that it was clear that F4 control the release of drug for definite period of time. Based on physiochemical evaluations and drug release profile, the formulation which is made from combination of polymers in the ratio of 25:25 was selected as optimised formulation.

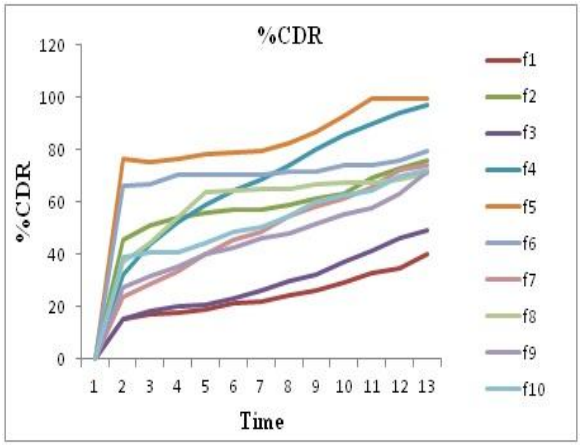

Figure 9: Graphical representation of %CDR

Table 23: Kinetic study of Ibuprofen from formulations F1-F10

Formulation	Zero order	First order	Higuchi	PEPPAS	
				n values	R^2values
F1	0.9546	0.9334	0.8796	0.8494	0.8494
F2	0.9436	0.9041	0.9055	0.1825	0.88
F3	0.9716	0.9483	0.9049	0.4694	0.8892
F4	0.9798	0.9106	0.9979	0.4427	0.9978
F5	0.8649	0.7081	0.8019	0.1229	0.6826
F6	0.8875	0.8596	0.8543	0.804	0.804
F7	0.9937	0.9868	0.9886	0.4824	0.9826
F8	0.9818	0.934	0.7272	0.3697	0.9076
F9	0.9818	0.934	0.9513	0.3697	0.9495
F10	0.9856	0.966	0.9365	0.2706	0.8709

Table 24: Kinetic study of optimised formulation F4

Time	%CDR	Square root of time	Log % of drug remaining to be released	Log time	Log % CDR
1	32.29	1	1.831	0.000	1.509
2	43.99	1.414	1.748	0.301	1.643
3	52.36	1.732	1.678	0.477	1.719
4	59.12	2	1.611	0.602	1.772
5	64.57	2.236	1.549	0.699	1.810
6	68.61	2.449	1.497	0.778	1.836
7	73.96	2.646	1.416	0.845	1.869
8	80.31	2.828	1.294	0.903	1.905
9	85.96	3	1.147	0.954	1.934
10	89.90	3.162	1.004	1.000	1.954
11	94.03	3.317	0.776	1.041	1.973
12	97.36	3.464	0.421	1.079	1.988

The best fit model for all the formulations were calculated and was observed that the formulation F4 followed Zero order kinetics while all others was fitting to peppas model. The release from the formulation followed non fickian diffusion as the diffusion exponent 'n' values less than 0.45 as per Korsmeyer and Peppa's model.

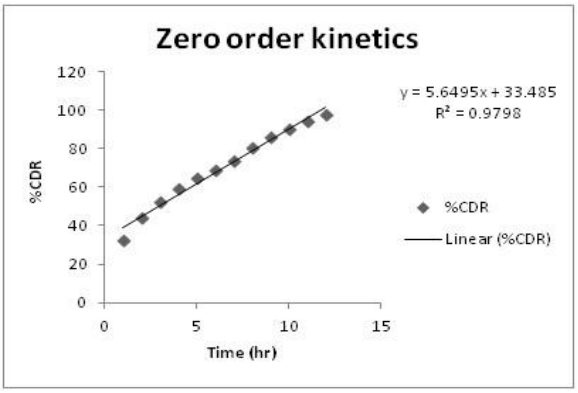

Figure 10: Zero order plot of formulation F4

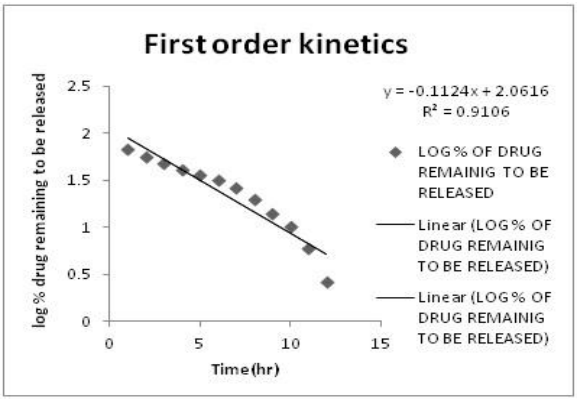

Figure11: First order plot of formulation F4

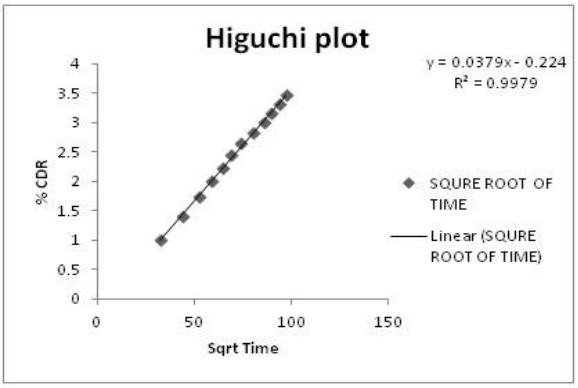

Figure12: Higuchi plot of formulation F4

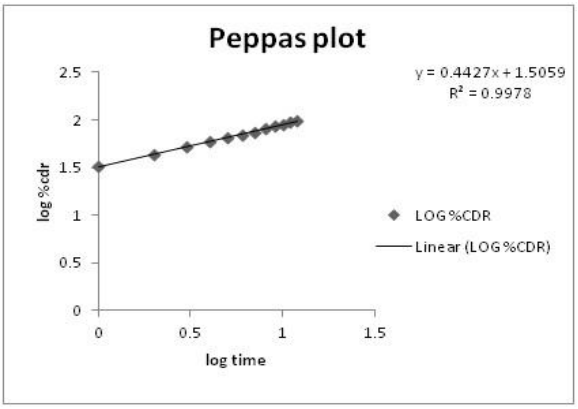

Figure 13: Peppas plot of formulation F4

Stability studies

Stability studies were carried out on formulations F4 for a period of 1 month and comparison of the parameters before and after stability studies were reported in the table.

Table 25: Comparison of physical parameters before and after stability

PARAMETERS	BEFORE STABILITY STUDIES	AFTER STABILITY STUDIES
PHYSICAL CHANGE	White, round	No change
%CDR	97.36	96.66
HARDNESS	5.63	5.61
THICKNESS	5	5

Table26: Drug release determination after stability

Time	%CDR	
	Before stability study	After stability study
1	32.29	32.39
2	43.99	43.49
3	52.36	51.26
4	59.12	55.19
5	64.57	60.64
6	68.61	64.57
7	73.96	73.75
8	80.31	79.10
9	85.96	85.96
10	89.90	89.49
11	94.03	93.93
12	97.36	96.66

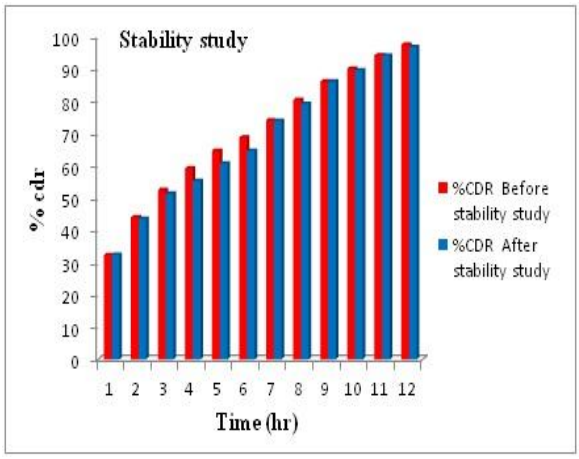

Figure14: Graphical representation of %CDR of stability study

From the stability studies it was found that there was no colour change in the formulation and stable in case of appearance and odour. But slightly decrease in drug release after 1 month. But it was not a large difference to affect the activity of formulation.

DISCUSSION

The result of study indicates that Okra gum powders have comparable effect with synthetic polymer and it has good efficiency in sustaining the drug release. The FTIR spectrum of okra polymer is same as that of HPMC. This shows the effectiveness of Okra gum powder. But the effect of okra gum is less as compared to HPMC but the combination in the ratio of 25:25 of okra and polymer shows more effective controlled drug release than HPMC. The moisture content of okra gum powder is less which indicates its stability. The cost required for the processing of okra pods to produce okra gum powder suggests that it can be marketed at much lower cost than that of other excipients.

Matrix tablet of Ibuprofen were formulated as controlled release tablets employing Okra powder and hydroxypropyl methylcellulose in different concentration and combination, and sustained release behavior of the fabricated tablets were investigated. Controlled released matrix tablets containing 250 mg Ibuprofen were developed using different drug: polymers combination. The angle of response and bulk density shows that the flow was well .The melting point shows that the Ibuprofen was pure.

Tablet prepared by direct compression method were subjected to physical characterization. The physical attributes of the tablet were found to be satisfactory. Typical tablet detects, such as capping, chipping & picking were not observed. Results for other physical evaluation were also found to be within an acceptable range. The drug content was within the range specified in IP. Formulation was optimized on the basis of acceptable properties and in-vitro drug release. In-vitro drug release was carried out using USP Type II at 50 rpm in 900 ml of phosphate buffer (pH 7.2) for 12hrs. Standard curve and withdrawal samples were analyzed in UV-VI spectrophotometry at 221nm.

CONCLUSION

The release mechanism and kinetics of a drug depends on the polymers used in formulations. Sometimes combination of one or more polymer is used. Wide varieties of synthetic polymers are now available most of them are expensive one. So the studies are concentrating to obtain less expensive and comparable effect when compared synthetic polymers.

The use of natural gums for pharmaceutical application is attractive because they are economical, readily available, non toxic, bio compatible. Lots of natural polymers from various plant sources have been successfully used and others are being investigated as excipient in design of dosage form for effective sustained release drug delivery. Tamarind gum, Okra gum, Hakea gum, Karaya gum, Fenugreek mucilage are some Plant sources for synthesis of polymer.

Results of the present study demonstrated that combination of both HPMC and Okra in the ratio of 25:25 can be successfully employed for formulating extended release tablet of Ibuprofen.

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