# EVALUATION OF SOME NATURAL POLYSACCHARIDES AS PHARMACEUTICAL EXCIPIENT FOR SUSTAINED RELEASE MATRIX TABLET

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**ABSTRACT:-**
The aim of this research work was to Evaluation of Some Natural Polymer used as Sustained Release Matrix Tablet, any pharmaceutical formulation contains two ingredients one is the active ingredient losartan Potasium and other is an excipients. In current senario, various plant have been studied for their diverse applications as excipients like binders, granulating agents, disintegrants, emulsifiers, suspending agents, gelling agents, mucoadhesive agents, matrix-formers, release retardants, enteric resistants, etc., in various pharmaceutical dosage forms. Among these, tamarind seed polysaccharide & okra mucilage is an emerging excipient, which is being used and investigated for the preparation of various dosage forms like suspensions, emulsions, tablets, gels, creams, etc. The current chapter deals with a comprehensive and useful discussion on extraction & isolation, chemical composition and properties of tamarind seed polysaccharide & okra mucilage.
In the tablet, Extended Release layer consist of Antihypertensive Drug belonging to class β-selective adrenergic blocking agent without partial agonist or membrane stabilizing properties. Extended release preparation provides sustained release and reduces the chances of tough related side effects. In selected cases of extended release preparation of this drug used in treatment of hypertension and congestive heart failure. The clinical studies have shown beneficial role of this drug as an extended release preparation. An excipients help in the manufacturing of dosage form and it also improves physicochemical parameters of the dosage form The main objective of the present study was to develop, formulate and evaluate a matrix tablet by using hydrophilic natural retardant polymers which would retard drug release in upper GI tract and should start releasing the drug when it reaches the alkaline environment of small intestine. Okara and Tramarind Gum Mucilage were investigated as the model hydrophilic retardant polymers. Nine batches of tablets were prepared. The prepared tablets were subjected for pharmacopoeial and non-pharmacopoeial evaluation parameters including loose and tapped bulk density, compressibility index, hausner ratio, angle of repose, friability, hardness, thickness, weight variation, % drug content and in-vitro drug release studies. It can be concluded that the combination of hydrophilic polymers that are retardant in nature are better suited for sustained and controlled drug delivery system than the hydrophilic polymer alone.

**Key Words**: Polymer, Sustained Release, Tablet, Drug, Extraction.

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## Introduction

Natural polymers or gums have been used in the preparation of release and controlled release drug dosage forms, because of their great properties, such as biodegradability, non-toxicity, biocompatibility in Nature and swelling when they come in contact with aqueous media. Tamarind (Tamarind indica L.) belongs to the Leguminosae family The oil extracted from its seeds is rich in eicosanoic fatty acids such as palmitic, oleic and linoleic, the highest concentrations corresponding to linoleic acid and palmitic acid, present in 36%–49% and 14%–20%, respectively Tamarind seed polysaccharide (TSP), is a natural branched polysaccharide polymer with a molecular weight of 700–880 kDa . Currently, an enormous numbers of plant polysaccharides have been isolated from various commonly available local plant source[1-2].Even these plant polysaccharides have been utilized in the formulation of various kinds of pharmaceutical products as excipients[4-5].Among various plant polysaccharides, tamarind seed polysaccharide is one of the emerging biopolymers, which is a galactoxylan extracted from the tamarind kernel and have found its wide and potential applications in food, cosmetic and pharmaceutical fields[7-8].Recent years, tamarind seed polysaccharide is being usedas useful pharmaceutical excipients in various dosage forms.

Plants produce a viscoelastic high-molecular-weight substance called mucilage. Mucilage is a polysaccharide-rich substance, but also contains proteins, minerals. Depending on the plant species, mucilage is secreted by roots, seeds, leaves, and stems. Mucilage secreted by seeds and roots has a variety of beneficial functions in the rhizosphere. For instance, the seed-coat mucilage increases the seed's water availability and resistance against drought, plays an important part in soil seed bank maintenance, and is utilized as a carbon source by beneficial rhizosphere microorganisms.

## Characteristics of an ideal pharmaceutical excipient

Pharmaceutical excipient should have some certain characteristics. Natural polymeric substances should have to fulfil these characteristics in order to be a successful candidate as pharmaceutical excipient. These are as follows:

1. Pharmacologically inert but pharmaceutically active.
2. Nontoxic and non-irritant.
3. No interaction with drug or with other substances present in the formulation and packaging.
4. Ease of handling.
5. Feasible.
6. Cost effective and readily available.

## Materials & Methods

Losartan potassium was obtained as a gift sample from Concept Pharma Aurangabad and other ingredients like okra gum & Xyloglucan were isolated & extracted was carried out at LSDP college laboratory (Pharmaceutics Research lab) Pune ,and other Excipients magnesium stearate, MCC PVP K-30 IPA,Talc. Purchased from Red Cross Formulation Pvt.Ltd, Sambhajinagar.

### Extraction of Okra gum:

About 2kg of fresh immature fruit of Abelmoschuse sculentus 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 Meta bisulphate. 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 desiccators. 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 us.

### Extraction TSP Extraction:

Cold distilled water (200 mL) was added to TSP powder (20 g) to prepare slurry. The slurry obtained was poured into boiling distilled water (800 mL) and then boiled for 20 min on a hot plate to give a clear solution that was stored overnight. The thin clear solution was further centrifuged at 6000 rpm for 20 min to separate all the foreign matter. The supernatant was separated and poured into excess 95% ethanol with continuous stirring. The obtained precipitate was collected using a stainless sieve, and dried in an oven at a temperature 50 °C for 4 h. The dried polymer was stored in a desiccator. In the same way, tamarind seed powder, waste from the export tamarind juice industry and were extracted using the procedure mentioned above. Only tamarind seeds taken from paddy farmland , were extracted by Accelerated Solvent Extraction (ASE) using methanol as a solvent, following by

ethanol, at a temperature of 100 ℃ for 30 min to give methanol extract (7.51%) and ethanol extract (3.31%).

**CHARACTERIZATION OF TAMARIND SEED POLYSACCHARIDE:**

**1.Solubility study:**

Solubility of the extracted Tamarind seed polysaccharide was evaluated qualitatively by stirring 10mg of Tamarind seed polysaccharide powder in 10 ml water, acetone, chloroform, and ethanol (1% dispersion). Solubility was determined by visual observation of the solute.

**2. PH Determination:**

1% W/V Tamarind seed polysaccharide dispersion of the sample in water was stirred consistently for 5 minutes and pH was determined using a pH meter.

**3. Viscosity study:**

Viscosity of Tamarind seed polysaccharide at 1% W/V concentrations was performed using the Brookfield viscometer (Model DV-E, U.S.A) with helipath stand. Viscosity of the polysaccharide dispersion was studied at a rotational speed at 10 rpm using a S-64 spindle in triplicate.

**4. Swelling ratio:**

One gram of Tamarind seed polysaccharide was placed into a 25ml glass Stoppard measuring cylinder. 25 ml of water was added into the cylinder containing polysaccharide and mixture was shaken thoroughly at intervals of every 10 min for 1 h. The sample was allowed to stand for 3 h at room temperature and volume occupied by mucilage was measured. The mean value was calculated, related to 1 g of polysaccharide .

**5. Fourier Transform Infrared Spectroscopy (FTIR):**

FT-IR spectrum of Tamarind seed polysaccharide, which presented peaks typical of the glycosidic structure of xyloglucans. The strong absorption peak at 3411 $cm^{-1}$ represents the hydroxyl (O-H) stretching vibration of polysaccharides and water involved in hydrogen bonding. The absorption peak at 2897 $cm^{-1}$ corresponds to the methylene group (C-H) stretching vibration peak characteristic of polysaccharides. The absorption peaks at 1647 $cm^{-1}$ and 1374 $cm^{-1}$ refer to the presence of carbonyl or carboxylic acid groups (C=O). The absorption peak at 1042 $cm^{-1}$ implies that TSP is pyran-glycosylated. In the anomeric region (950–700 $cm^{-1}$), the polysaccharide exhibited an obvious characteristic absorption at 897 $cm^{-1}$, which was assigned to D-galactopyranose. The absorption peak at 944 $cm^{-1}$ could represent D-glucopyranose.

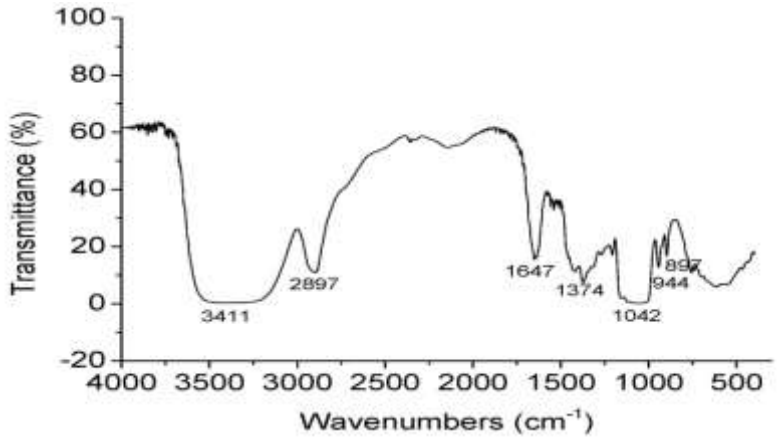



**Fig 1. FTIR Spectra of Tamarind Seed Polysaccharide**

**CHARACTERIZATION OF OKRA MUCILAGE:**

**1. Solubility study:**

Solubility of the extracted mucilage was evaluated qualitatively by stirring 10mg of Okra powder in 10mL water, acetone, chloroform, and ethanol (1% dispersion). Solubility was determined by visual observation of the solute.

**2. $P^H$ Determination:**

1% W/V okra mucilage dispersion of the sample in water was stirred consistently for 5 minutes and pH was determined using a pH meter.

**3. Viscosity study:**

Viscosity of Okra gum at 1% W/V concentrations was performed using the Brookfield viscometer (Model DV-E, U.S.A) with helipath stand. Viscosity of the mucilage dispersion was studied

at a rotational speed at 10 rpm using a S-64 spindle in triplicate.

**4. Swelling ratio:**

One gram of mucilage was placed into a 25ml glass Stoppard measuring cylinder. 25 ml of water was added into the cylinder containing mucilage and mixture was shaken thoroughly at intervals of every 10 min for 1 h. The sample was allowed to stand for 3 h at room temperature and volume occupied by mucilage was measured. The mean value was calculated, related to 1 g of mucilage (Srinivas et al., 2003).

**5. Fourier Transform Infrared Spectroscopy (FTIR):**

FTIR spectra were recorded of polymer (Okra mucilage). The samples were analyzed by KBr pellet method using FTIR spectroscopy. The spectra were scanned over a frequency range 4000-400 cm−1.

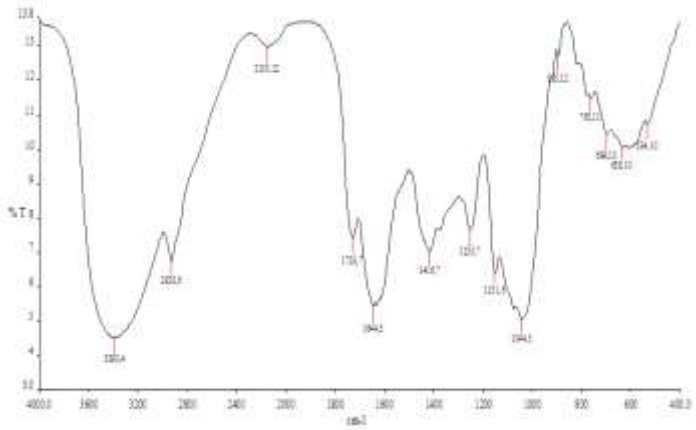


**Fig 2. FTIR Spectra of Okra Mucilage**

For preparing the matrix tablets, Losartan potassium and various concentration of Xylogucan and okra gum were used as a hydrophilic polymer.The other excipient used was MCC for its diluent property. They were first sieved and then sufficient amount of Isopropyl alcohol was added and then wet mass was sieved through mesh no.20 and dried at 55 c for 1hr in an oven. The dried granules were passed through mesh no.16 and fractions of granules retained on the sieve were discarded. Finally, 1% talc and0.5% magnesium stearate was mixed for lubrication of granules which were then compressed by cadmach single punch machine by using 9.5mm flat punch. The weight of tablet was adjusted to 250 mg and each tablet contained 50 mg Losartan potassium. The compressed tablets of each type of polymer were then evaluated for tablet characteristics such as thickness, weight variation and friability.

**Preparation of matrix tablets by Wet Granulation method**

The sustained release matrix tablets of Losartan potassium tablet were prepared by wet granulation method. Shows the composition of each matrix formulation. The formulation of each Losartan potassium sustained release matrix tablets is composed of two selected polymers i.e. Xyloglucan, and okra gum in alone or in combination. The other excipients used were MCC for its diluent property, PVP K-30 as a binder and magnesium stearate and talc. The weight of tablet was adjusted to 250 mg and each tablet contained 50 mg Losartan potassium**.** Total 9 batches (F1-F9) were prepared.

Batch F1, F2 and F3 containing a single polymer i.e.Xyloglucan in concentration of 15, 20 and 25% of total weight of the tablet. Batch F4, F5 and F6 containing a single polymer i.e. okra gum in concentration of 20, 30 and 40% of total weight of the tablet. Batch F7, F8 and F9 containing combination of both polymers i.e. okra gum & Xyloglucan in concentration of proportion ratios of 10:10, 15:15 and 20:20% of total weight of the tablet respectively.

All the powders were passed through 60 mesh sieve after sieving. The drug & polymer were mixed uniformly, MCC was added to the above mixture and blend for 20 min. PVP K-30 dissolved in isopropyl alcohol (3%) was then added to the above mixture to form a wet mass. The wet mass was then passed through sieve no. 16 and granules were dried for 2 hrs at 55-60$^0$C. After drying, granules were passed through 20 mesh screen (1.18 mm sieve) and resulting granules were mixed with magnesium stearate (1%) and talc (2%). The lubricated granules were compressed using 9.5 mm flat faced round punches (single punch tablet machine) into

tablets. Compression pressure was adjusted during

Tablet formulating of each formula to get the tablet hardness in the range of 5 to 5.6 kg/cm$^2$. The compressed tablets of each formulation batch were then evaluated for tablet characteristics such as thickness, hardness, weight variation, friability and drug content.

**Preparing the SR Matrix Tablets:**

For preparing the matrix tablets, Losartan potassium and various concentrations of Okara and Tramarind Gum Mucilage Xyloglucan were used as a polymer. The other excipient used was MCC for its diluents property. They were first sieved and then sufficient amount of Isopropyl alcohol was added and then wet mass was sieved through mesh no.20 and dried at 55 c for 1hr in an oven. The dried granules were passed through mesh no.16 and fractions of granules retained on the sieve were discarded. Finally 1% talc and0.5% magnesium stearate was mixed for lubrication of granules which were then compressed by cadmach single punch machine by using 9.5mm flat punch. The weight of tablet was adjusted to 250 mg and each

**Table 1. Formulation of SR Matrix Tablet**

| **Ingredient** | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** | **F9** |
|---|---|---|---|---|---|---|---|---|---|
| Losartan Potassium | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| Xyloglucan | 50 | 75 | 100 | | | | 25 | 37.5 | 50 |
| Okra gum | | | | 50 | 75 | 100 | 25 | 37.5 | 50 |
| MCC | 135 | 115 | 85 | 135 | 115 | 85 | 135 | 115 | 85 |
| PVP K-30 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| IPA | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s |
| Mag.Sterate | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Talc | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| **Total Weight** | **250** | **250** | **250** | **250** | **250** | **250** | **250** | **250** | **250** |

**Result and Discussion:**

**A. drying of Losartan potassium**

The pharmacopoeia limits for LOD of losartan potassium reported not more than 1% and the experimental values for given sample of losartan potassium where found to be 0.67% indicating good agreement between the reported and experimental value.

**B. Selection of Excipients:**

**Table No 2.: Selection of Excipients.**

| **Sr.No.** | **Ingredient** | **Category** |
|---|---|---|
| 1. | Xyloglucan | Sustain relese matrix polymer |
| 2. | Okra gum | Sustain release matrix polymer |
| 3. | Microcrystaline cellulose | Diluent |
| 4. | PVP K-30 | Binder |
| 5. | Isopropyle alcohol | Binder |
| 6. | Magnesium stearate | Glident |
| 7. | Talc | Lubricant |

**C. Characterization of Losartan potassium**

**Table No.3: Organoleptic characterization and Melting point determination.**

| **Test** | **Observation** |
|---|---|
| Colour | White,crystalline powder |
| Odour | Odorless |
| Test | Bitter |
| Melting point | 184$^{O}$C |

**D: Solubility Analysis:**

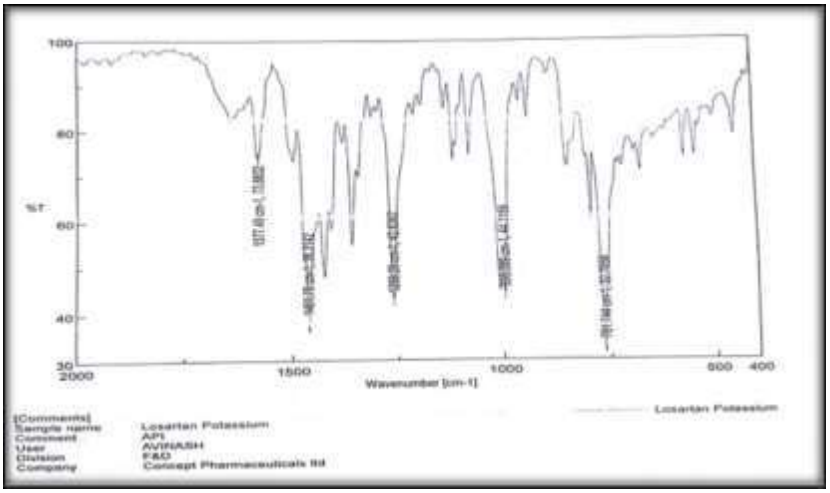
**Table No.4: Solubility profile of Losartan potassium**

| **Sr.No** | **Solvent** | **Solubility** |
|---|---|---|
| 1. | Distilled water | Soluble |
| 2. | Chloroform | Insoluble |
| 3. | Methanol | Soluble |
| 4. | Ethanol | Soluble |

**E.: Micrometrics characterization of drug:**

**Table No.5 : Micrometrics characterization of Losartan potassium :**

| Sr. No. | Parameter | Result |
|---|---|---|
| 1. | Loose bulk density | 0.3942gm/cm$^3$ |
| 2. | Tapped density | 0.4454gm/cm$^3$ |
| 3. | Carrs Index | 15.37% |
| 4. | Hauners ratio | 1.1817 |
| 5. | Angle of repose | $31^0 21'$ |




**F. Compatibility studies of Drug and Polymers:**

**Figure 3. IR Spectrum of Losartan Potassium.**

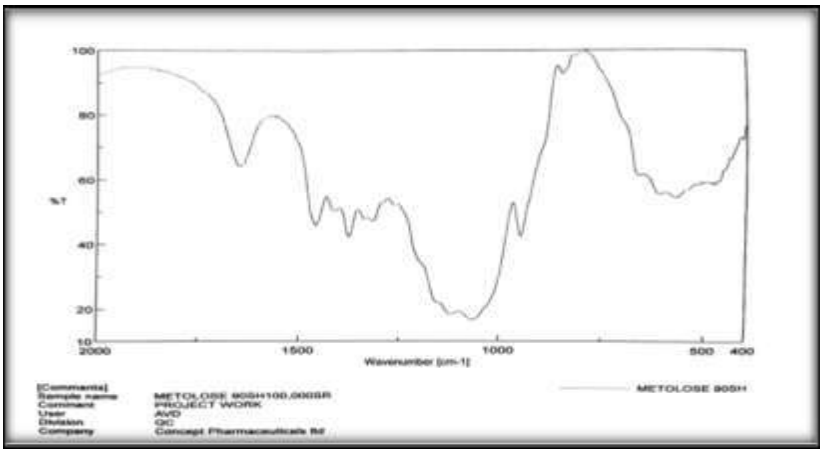



**Figure 4. IR Spectra of Okara gum.**

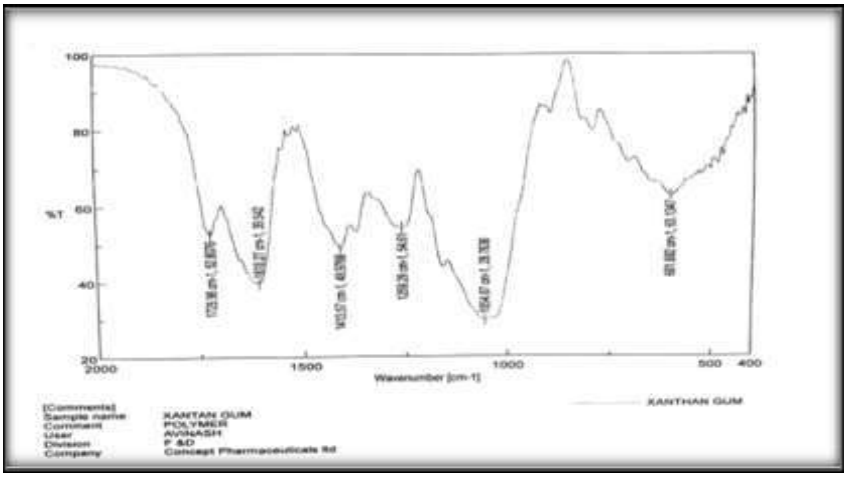



**Figure 5. IR spectra of Tramarind Gum Mucilage.**

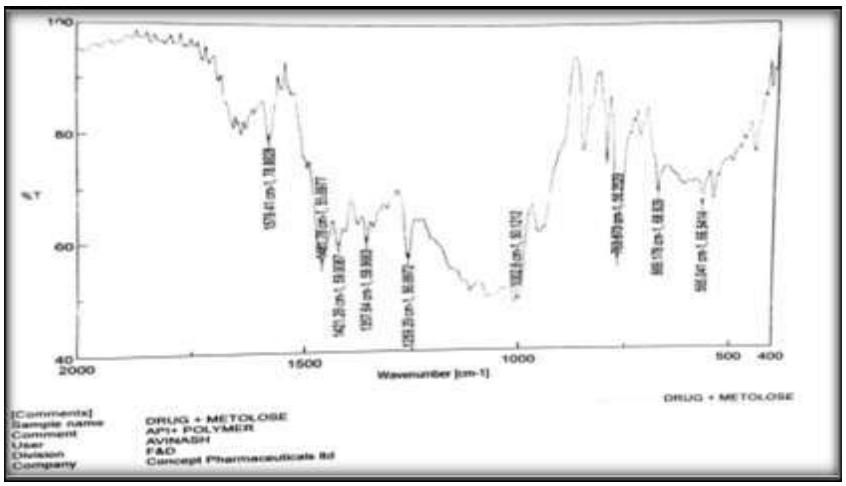



**Figure 6.IR Spectra of Drug with Okra**

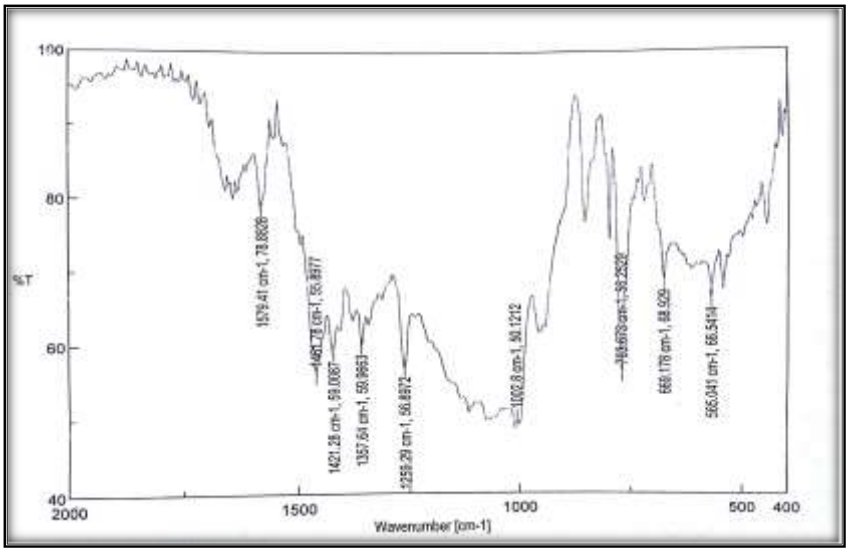



**Figure 7**. **IR Spectra of Drug with Xyloglucan& okra gum**

**Evaluation of Losartan Potassium SR Matrix Tablets.**

**Table No.6.Standard physical test for matrix tablets.**

| Formulation | Hardness (kg/cm$^{2)}$ | Percent Friability (%) | Thickness (mm) | Content Uniformity (%) | Weight variation |
|---|---|---|---|---|---|
| **F1** | 5.10.1 | 0.57±0.03 | 3.50.2 | 101.20% | 2520.55 |
| **F2** | 5.00.1 | 0.69±0.03 | 3.70.2 | 99.63% | 2500.47 |
| **F3** | 5.20.2 | 0.49±0.04 | 3.50.1 | 98.93% | 2480.57 |
| **F4** | 5.20.1 | 0.65±0.02 | 3.50.2 | 98.28% | 2510.20 |
| **F5** | 5.00.2 | 0.51±0.06 | 3.80.4 | 96.60% | 2480.43 |
| **F6** | 5.20.1 | 0.62±0.04 | 3.70.3 | 89.94% | 2500.52 |
| **F7** | 5.10.2 | 0.67±0.06 | 3.80.4 | 97.23% | 2510.20 |
| **F8** | 5.30.1 | 0.68±0.01 | 3.50.2 | 98.16% | 2490.81 |
| **F9** | 5.00.2 | 0.55±0.05 | 3.70.3 | 99.11% | 2500.51 |

* **All the values represent mean** standard **(n=3).**

Tablets of all formulations (F1 to F9) were evaluated for different parameters such as thickness, hardness, weight variation, drug content and friability and results shown in table.

**1. In-Vitro Release Studies**

**Table No.7 In Vitro Dissolution data of F1, F2, and F3 Formulation.**

| Times in (Hrs) | Cumulative Percent drug release | | |
|---|---|---|---|
| | **F1** | **F2** | **F3** |
| 0 | 0 | 0 | 0 |
| 1 | 21.52 | 21.38 | 19.14 |
| 4 | 37.74 | 38.27 | 34.46 |
| 8 | 76.18 | 79.24 | 70.49 |
| 12 | 99.20 | 98.07 | 89.93 |

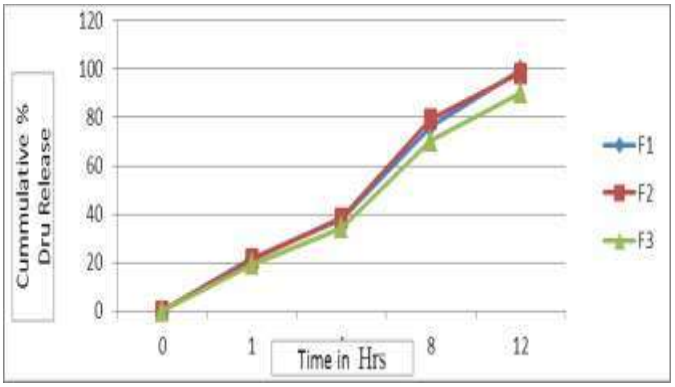



**Figure 8. : In-vitro dissolution profile of F1, F2 and F3 Formulation.**

**Table No.8 In Vitro Dissolution data of F4, F5, and F6 Formulation.**

| Times in (Hrs) | Cumulative Percent drug release | | |
|---|---|---|---|
| | **F4** | **F5** | **F6** |
| 0 | 0 | 0 | 0 |
| 1 | 17.93 | 19.14 | 14.94 |
| 4 | 36.10 | 37.77 | 30.23 |
| 8 | 74.56 | 78.60 | 70.48 |
| 12 | 94.28 | 95.79 | 86.94 |

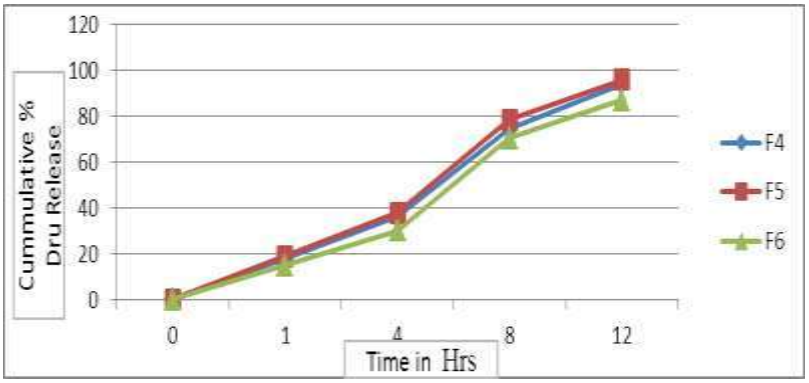



**Figure 9.: In-vitro dissolution profile of F4, F5 and F6 Formulation.**

**Table No.9.In-Vitro Dissolution data of F7, F8 and F9 Formulation.**

| Times in (Hrs) | Cumulative Percent drug release | | |
|---|---|---|---|
| | **F7** | **F8** | **F9** |
| 0 | 0 | 0 | 0 |
| 1 | 19.24 | 21.28 | 23.15 |
| 4 | 31.64 | 34.52 | 37.49 |
| 8 | 71.21 | 73.14 | 75.32 |
| 12 | 96.23 | 97.16 | 99.11 |

**CONCLUSION:-**

Xyloglucan & Okra gum is Natural polymers which have been used in different pharmaceutical formulations. The overall study carried out on instruments mixture and grinder, Hot air oven and sieves are used for formation of powder. Characterization of Tamarind Seed Polysaccharide (Xyloglucan) and okra fruits with study of Solubility, pH Determination, Viscosity study, swelling ratio and FTIR. The pH was found to be 6.5 and 6.1 for Okra mucilage and Tamarind Seed Polysaccharide respectively. The result of the present study demonstrated the isolated tamarind seed polysaccharide& Okra mucilage can be used as a drug release retardant, which was evident, from the results. The current chapter demonstrates the possibilities of using tamarind seed polysaccharide & Okra seeds as promising pharmaceutical excipients in various pharmaceutical formulations such as sustained release, controlled release tablets. All the prepared formulation containing different concentrations of Xyloglucan and okra gum. The prepared formulations satisfy all pharmacopoeia standards. The concentration of Xyloglucan and okra gum increases an increase in the viscosity of the gel as well as the formation of gel layer with a longer diffusion path.

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