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Formulation and Evaluation of Sustained Release Matrix Tablet of Antiviral Drug by Natural polysaccharide

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Abstract : The aim of this investigation was to develop and optimize Antiviral matrix tablets for sustained release application. The sustained release matrix tablet of Acyclovir was prepared by wet granulation technique using Colocasia esculenta corms polysaccharide. The polysaccharide obtained after extracted from natural source and evaluated for their colour, viscosity and pH.The prepared tablet was evaluated for their hardness, friability, drug content, *In vitro* dissolution, swelling studies. Effect of different natural polymers on the drug release from the tablet was studied. The optimized Formulation F-1 shows up to 97% of drug release in 720 min. whereas formulation F-6 shows 85 % of drug release in 720 min. which shows Formulation F-1 and F-6 shows the sustained release of drug up to extended time. The drug release from the tablet was sustained and non-Fickian transport of drug from the tablet was confirmed. Using Higuchi's Model and the Korsmeyer equation, the drug release mechanism from the sustained release tablets was found to be Anomalous (non-Fickian) diffusion. Compatibility study confirmed that interactions do not exist between the drug and polymer.
Keywords: *Acyclovir, matrix tablet, Sustained Release, Colocasia esculenta, Natural Polymer.*

Introduction –

Historically oral drug administration has been the predominant route for drug delivery. Oral route has been one of the most popular routes of drug delivery due to its ease of administration, patience compliance, least sterility constraints and flexible design of dosage forms. It is known to be the most popular route of drug administration due to the fact the gastrointestinal physiology offers more flexibility in dosage form design than most other routes. Some drugs are enclosed in polymer based tablets with a laser drilled hole on one side and a porous membrane on the other side. Stomach acids push through the porous membrane, thereby pushing the drug out through the laser drilled hole. In time, the entire drug dose releases into the system while the polymer container remains intact, to be later excreted through normal digestion.[1-3]

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Drawbacks of Conventional Dosage Forms [**4]**

Poor patient compliance, increased chances of missing the dose of a drug with short half-life for which frequent administration is necessary.The unavoidable fluctuations of drug concentration may lead to under medication or over medication.

Advantages of sustained release dosage forms:

A typical peak-valley plasma concentration time profile is obtained which makes attainment of steady-state condition difficult. Sustained-release oral delivery systems are designed to achieve therapeutically effective concentrations of drug in the systemic circulation over an extended period of time. Possible therapeutic benefits of a properly designed SR dosage form include low cost, simple processing, improved efficacy, reduced adverse events, flexibility in terms of the range of release profiles attainable, increased convenience and patient compliance. [**5,6]**

Material and Methods –

Fresh Colocasia esculenta corms were bought from local market for the extraction of the polysaccharide. Acyclovir was received as a gift sample from Quimica Sintetica , S. A., Mumbai. Lactose monohydrate, Magnesium stearate and Talc purchased fromSunchem and Lobachemie pvt.Ltd. Mumbai other excipients used to prepare the tablets were of standard pharmaceutical grade and all other chemical reagents used were of analytical grade.

Experimental

Extraction and evaluation of natural polysaccharide [**7,8]**

The natural polymer from the respective natural source (Colocasia esculenta corms) were extracted following the method described here. In this method, About 200 gm of Fresh taro corms were washed to polish off the adherent soil material later peeled and Soaked in water for 12 hour and made in a smooth paste. Taro corm paste was suspended in 1% NaCl solution and stood for 1 hour. The slurry was passed through a muslin cloth . The filtrate was collected and an equal amount of acetone was added and stirred for few minutes, the mucilage was carefully separated. The mass then dried in a tray drier until it completely dried. After complete drying the powder was sieved using mesh #20 and stored for further use.

Colour:

After complete extraction and drying the polysaccharide were evaluated for colour by visualization.**[9]pH**: A 1%w/v solution of the polysaccharide were prepared and its pH were measured in digital pH meter. [**10]Viscosity**: The viscosities of 1% w/v solution of the polysaccharide were measured in Ostwald viscometer. [**11]**

Preparation of Matrix Tablets [**12-13]**

Tablets containing Acyclovir were prepared by wet granulation technique using the formula given in the table 1. Acyclovirsustained release matrix tablets were prepared with natural polysaccharide and other additives. Acyclovir and lactose were mixed together, and granulate it with the natural polysaccharide solution until a wet mass was obtained. Then the coherent mass was passed through #22 and the granules were dried at 40 + 2 °C for 2 hours. Dried granules were passed through #44 and lubricated it with magnesium stearate and talc was added to the granules. Then the lubricated granules were compressed into tablets using tablet punching machine. The compressed tablets were dedusted and evaluated for various tablet properties.

Table 1 Formulation of Acyclovir Matrix Tablets Using Taro polysaccharide

Ingredients	F1	F2	F3	F4	F5	F6
Drug	200	200	200	200	200	200
Lactose	240	190	165	140	115	90
Taro Polysaccharide	50	100	125	150	175	200
Talc	5	5	5	5	5	5
Magnesium stearate	5	5	5	5	5	5

All quantities were in milligrams All the batches contained 1.0% w/w talc and magnesium stearate

Evaluation of prepared matrix tablet of Acyclovir

Pre-compression characteristics [**14-15]**

All the formulation prepared was evaluated for Angle of repose, Bulk density, and Compressibility index.

Post-compression characteristics [**16-17]**

All the formulation prepared were evaluated for Weight variation test, Thickness and diameter, Hardness and Friability test.

Drug content [**18]**

Five tablets were weighed individually and powdered. The powder equivalent to average weight of tablets was weighed and drug was extracted in 0.1N HCl, the drug content was determined measuring the absorbance at 255 nm after suitable dilution using a UV- Vis double beam spectrophotometer Shimadzu 1800, Japan.

***In vitro* dissolution study of tablet** [**19-21]**

The in vitro release of Acyclovir from the formulated tablets was carried out in Tablet dissolution tester USP- Electro lab USP- TDT- 08L using 900 ml of dissolution medium maintained at 37.0 ±0.5°C and a stirring rate of 100 rpm. Six tablets from each formulation were tested individually in simulated gastric fluid (pH 1.2) for the first 2 h and in phosphate buffer (pH 6.8) for the following 10 h. At every 1 h interval, samples of 5 ml were withdrawn from the dissolution medium and replaced with fresh medium to maintain the volume constant. After filtration and appropriate dilution, the amount of DS resent in each sample was determined Spectrophotometricallyat 255 nm.

Compatibility Studies [**22]**

Compatibility with excipients was confirmed by FTIR studies. The pure drug and its formulations along with excipients were subjected to IR studies.

Results and Discussion

Characterization of natural polysaccharide –

The polysaccharide obtained after extraction white in colour (colocasia esculenta). The viscosity was found to be 1.1152 cps. The pH was found to be 6.5.

Pre-Compression Characterization of Acyclovir Matrix Tablet-

The angle of repose for the formulated blend was carried out and the results were shown in table 2 It concludes all the formulations blend was found to be in the range from 20-25 its indicate well to passable flow

of granules. Compressibility index was found in the range from 13.04 % -28.57 % indicating the powder blend has the excellent to good flow property for compression.

Table 2 Pre& Post Compression Characterization of AcyclovirMatrix Tablet

Batch No.	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's Index (%)	Housner Ratio	Angle of Repose (°)	Weight Variation (Av. wt) (n=20)	Hardness kg/cm^2 (n=3)	Friability (%) (n=20)	Drug Content (%) (n=3)
F-1	0.51	0.66	22	1.29	25	0.499	7.66	0.86	99.18
F-2	0.5	0.706	28.57	1.41	24	0.488	5.33	0.97	98.65
F-3	0.66	0.759	13.04	1.150	20	0.492	6.33	0.78	99
F-4	0.66	0.779	15.27	1.180	22	0.496	7.66	0.65	98.20
F-5	0.625	0.781	19.97	1.25	21	0.498	6.66	0.36	97.76
F-6	0.571	0.751	23.96	1.31	24	0.488	7.33	0.56	98.11

where n is number of Tablets.

Post-compression characterization of Acyclovir matrix tablet

Microscopic examinations of all the tablets formulations were found to be circular shape with no cracks. The measured hardness of tablets of each batch ranged between 5.33 to 7.66 kg/cm^2(Table 2). This ensures good handling characteristics of all batches. The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

The percentage weight variations for all formulations were tabulated in Table 2**.** All the formulated tablets passed weight variation test as the Avg. weight variation was within the Pharmacopoeial limits of ±7.5% of the weight. The weights of all the tablets were found to be uniform with low standard deviation values. **Drug Content (%)** -The drug content for all the formulated tablets was found to 97.76% to 99.18 % of Acyclovir. It complies with official specifications.

***In vitro* drug release study-**

In vitro drug release profile of the prepared Acyclovir Matrix tablets was studied. The release data obtained from all the formulations shown in fig.1. The release of drug from the Tablet exhibited a sustained & controlled pattern over an extended time period. The tablet formulation F-1 was found to release the drug of about 97.40% after 12 hrs, The tablet formulation F-6 was found to release the drug of about 85.33% after 12 hrs, thus concluded to have sustained drug release for longer period of time in sustained and controlled pattern.

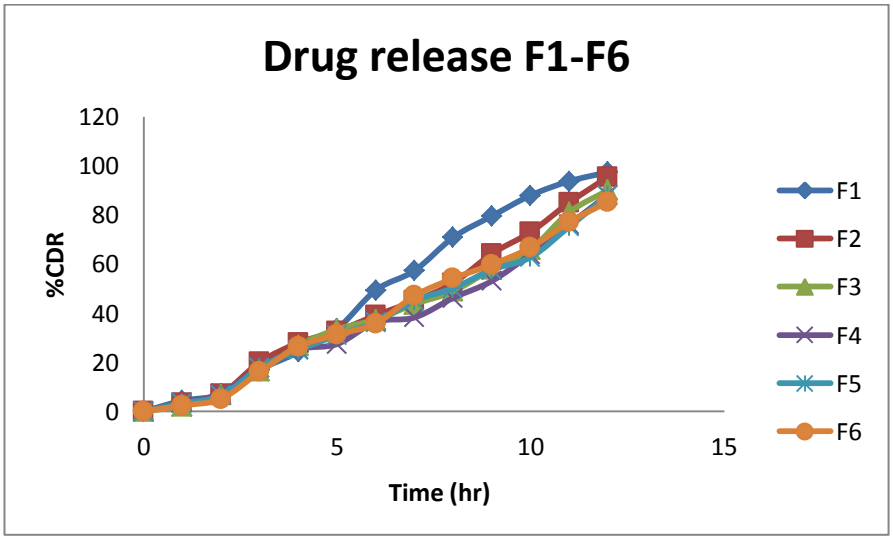


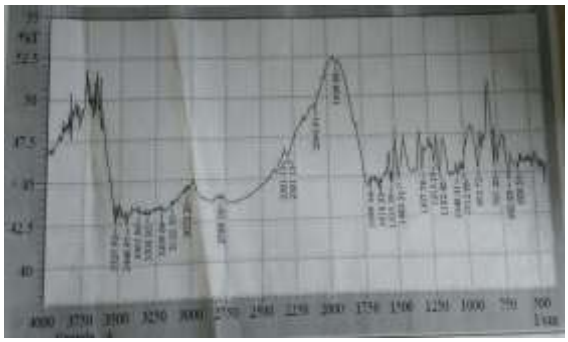
Fig. 1 *In-vitro* drug release kinetics data for formulation using taro polysaccharides

Drug Polymer Compatability Study

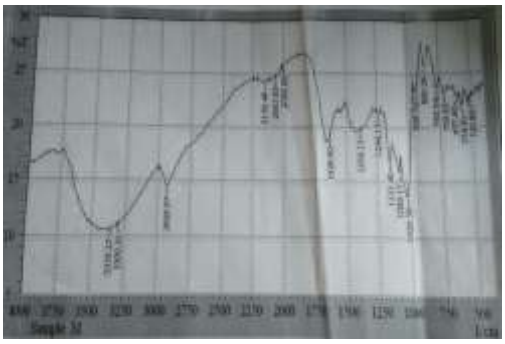
Fourier Transform Infrared Spectroscopy (FTIR)

Compatibility study of drug and Polysaccharide was conducted by employing I.R. Spectral studies. The IR spectrum of Acyclovir, Taro gum and their physical mixtures are shown in Figure The following characteristic peaks were observed with Acyclovir C=N- (stretching) 1699.34,cm-1, C-N- (stretching) 1535.39, cm-1, N-H- (stretching) 3446.91,cm-1. As the identical principle peaks were observed in all the cases,

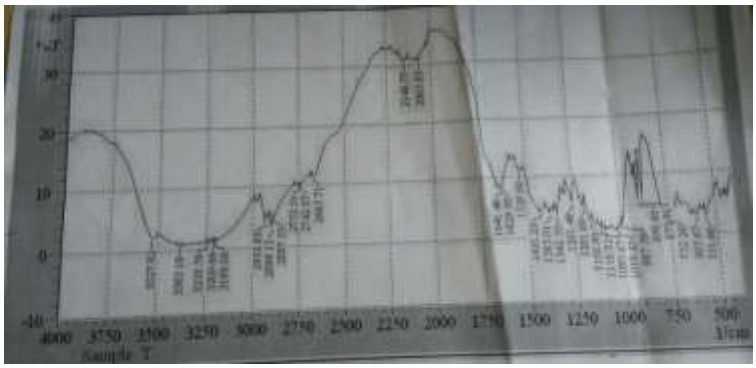
Hence it shall be confirmed that interactions do not exist between the drug and polymer.



(a)



(b)



(c)

Fig.2 FTIR spectra showing (a) Acyclovir(b) Taro polysaccharides(c) Physical mixture of drug and excipients

Conclusion-

This study deals with the investigation carried out with the objective of developing oral sustained release formulations through matrix tablets for widely used Antiviral drug Acyclovir using natural gum as Taro gum and evaluation of their sustained release potential. Based on results and discussions, it is concluded that the formulated matrix tablets of acyclovir using natural gum and lactose were capable of exhibiting sustained release properties. They are thus capable of reducing the dose intake, minimize the blood level oscillations, dose related adverse effect and cost thus ultimately improve the patient compliance in the therapeutic management of pain and inflammation. The F5 and F6 formulations exhibited best Binding properties for the sustained release character.

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