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Formulation and evaluation of sustained Release Isoniazid Tablet effect of natural polysaccharide on drug release mechanism

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Abstract : The aim of this study was to evaluate the binding efficiency of mucilage extracted from *Dioscorea alata* (water yam). The sustained release matrix tablet of Isoniazid was prepared by wet granulation technique using *Dioscorea alata* Linn. polysaccharide. The polysaccharide was extracted from the tuber via maceration method and evaluated for their color, viscosity and pH. The prepared tablet was evaluated for their hardness, friability, drug content, swelling studies and In vitro dissolution rate. Optimized Formulation F2 and F3 was exhibited satisfactory results as 95 % and 91 % in 12 hrs. whereas formulation F-5 shows 85 % of drug release in 12 hrs. 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 : Isoniazid matrix tablet, Sustained Release, *Dioscorea alata* linn. Polysaccharide.

Introduction-

Now a day's most of the pharmaceutical scientists are involved in developing an ideal drug delivery system. This ideal system should have advantage of single dose for whole duration of the treatment and it should deliver the drug directly at specific site. scientists have success to develop a system that can be as near to an ideal system. The design of oral sustained drug delivery system should be primarily aimed to achieve the more predictability and reproducibility to control the drug release, drug concentration in the target tissue and reproducibility to control the drug release and drug concentration. This system will provide actual therapeutic control that would be temporal (time related), spatial (site related) or both. Sustained-release formulation are helpful in increasing the efficiency of the dose as well as they are also improving the patient's compatibility. [1-4].

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Materials

Fresh Yam tuber were bought from local market for the extraction of the polysaccharide. Isoniazid and Lactose was received as a gift sample from Lobachemie pvt. Ltd. Mumbai. Magnesium stearate and Talc purchased from Sunchem, India. Other excipients were used to prepare the tablets of standard pharmaceutical grade and all other chemical reagents used were of analytical grade.

Experimental

Extraction and evaluation of polysaccharide from Tuber

The yam tuber was peeled and weighted. The 500 gm weighed yam was cut into small pieces. Then the yam pieces was blended with 1.5 liter distilled water which contain 0.33 % sodium metabisulphite. The slurry was kept in a beaker for 25 minute. After that supernatant layer was separate in another beaker. The yam mucilage was precipitated from supernatant using Acetone in ratio of 2 : 1 . Mixed properly with glassrod. This solution was kept in a Hot air oven at 50 °C for One hour. Than filter the solution and separate the precipitated mucilage. After filtration it was dried in Hot air oven at 60°C in petridish for 25 minutes. The dried mucilage was crushed and powdered; The crushed powder put in air tight container. [6]

Color :

After complete extraction and drying the polysaccharide were evaluated for color by visualization. **pH:** A 1%w/v solution of the polysaccharides were prepared and its pH were measured in digital pH meter. **Viscosity:** The viscosities of 1% w/v solution of the polysaccharides were measured in Ostwald viscometer. [7]

Preparation of Matrix tablets

Sustained Release tablets of Isoniazid were prepared by wet granulation method. The drug: polymer ratios are 1:0.5, 1:1, 1:1.5, 1:2, 1:2.5 respectively used. The natural polysaccharide was used as matrix forming material. All ingredients were weighed accurately. Than mixed together for 10 minutes in polybag and mixture was passed. Now wet mass prepared using small quantity of distilled water as a moistening agent. The wet mass was passed through a screen (mesh size 18) and granules were dried in a Hot air oven at 45°C for 2 hours. When granules were dried again passed to sieve 18. The tablets were compressed using hand operating machine. [8]

Table 1: Formulation of SR matrix tablet of Isoniazid using natural polysaccharide.

Ingredients	F1	F2	F3	F4	F5
Drug (Isoniazid)	100	100	100	100	100
Polysaccharide (DA)	50	100	150	200	250
Lactose	340	290	240	190	140
Magnesium stearate	5	5	5	5	5
Talc	5	5	5	5	5

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

Evaluation of SR matrix tablet

Pre compression characteristics [9,10]

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

Post compressive characteristics[11-13]

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

Drug content[14]

Transfer One finely powdered tablet to a 100 ml volumetric flask with buffer 6.8 pH of phosphate solution. One ml of solution withdraw from flask and transfer into another volumetric flask and dilute with buffer solution. The amount of Isoniazid present in each sample solution was determined by UV spectrophotometer at 263 nm. This procedure was repeated trice and this average was chosen.

In vitro dissolution study of tablet[15]

The *in-vitro* dissolution study was determined as per USP XXIV. The rotating paddle method was used for study of drug release from tablets. The dissolution medium consisted 900ml of 0.1 N HCl and 6.8 pH buffer solution. The release was performed at 37 °C ± 0.5 °C, at 50 rpm rotation. Five ml of solution was withdrawn at specified time interval and maintain sink condition. The absorbance of withdrawn sample was measured by UV spectrophotometer at 263 nm.

Compatibility Studies[16]

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 polysaccharides –**

The polysaccharides obtained after extraction of tuber was light brown in color. The viscosity was found to be 1.10cps. The pH were found to be 6.7.

Pre-Compressive Characterization of Isoniazid 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 21°-25° its indicate well to passable flow of granules. Compressibility index was found in the range from 15%- 16.9 % indicating the powder blend has the excellent to good flow property for compression.

Table 2- Pre And Post Compression Characterization of Isoniazid Matrix Tablet

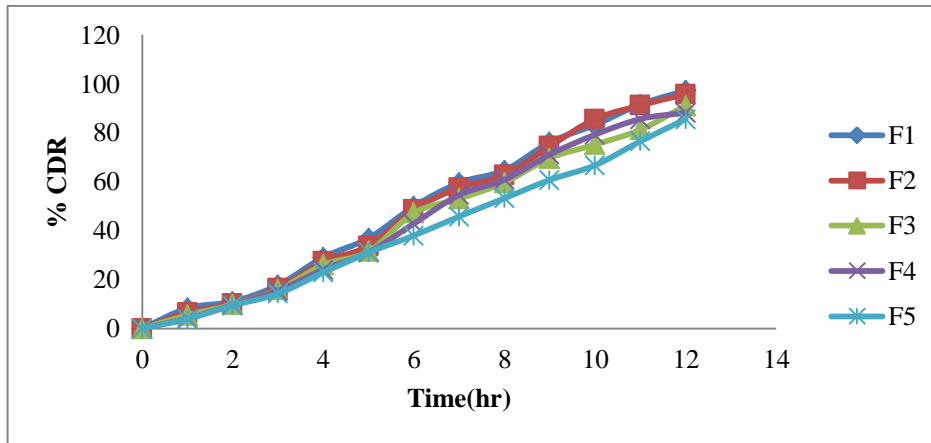
Batch	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index	Angle of repose	Hausner ratio	Weight variation (mg)	Hardness (Kg/cm ²)	Thickness(mm)	Friability (%)	Drug content (%)
F1	0.51	0.60	15	21.30	1.17	499.33	5.33	0.8	0.86	97.38
F2	0.42	0.50	16	22.78	1.19	502.33	5	0.9	0.95	96.39
F3	0.54	0.65	16.9	21.80	1.20	498.66	4.3	0.9	0.93	97.63
F4	0.60	0.68	11.76	25.64	1.13	499	5.3	0.8	0.56	97.5
F5	0.51	0.60	15	24.22	1.17	498.66	6.3	0.9	0.32	99.25

Post-compression characterization of Isoniazid 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 4.3 to 6.3 kg/cm²(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 % 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 97.38% to 99.25 % of Isoniazid. It complies with official specifications.

In vitro drug release study-

In vitro drug release profile of the prepared Isoniazid 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 pattern over an extended time period. The tablet formulation F1 was found to release the drug of about 97% within 12hrs, The tablet formulation F3 and F4 was found to release the drug of about 91% and 88% after 12 hrs, thus concluded to have sustained drug release for longer period of time in sustained and controlled pattern.



Graph No. 1: - *In vitro* drug release profile of the prepared Isoniazid tablets Batch F1-F5

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 Isoniazid, Polysaccharide and their physical mixtures are shown in Figure. The following characteristic peaks were observed with Isoniazid as well as the formulations containing Yam polysaccharide. Stretching at 1602.4 around and N-H stretching band around 3304.1. Ring C-C-H sym bending on 844.85, C-N stretching bend at 1334.78 and C-C-H bending at 887.28 around. 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)
Figure-(a)FTIR of Polysaccharide,(b)Isoniazid and (c)mixture of drug and excipients

Conclusion

In these studies it was found that the tuberculosis is highly contagious bacterial disease caused by mycobacterium tubercle bacilli. The sustained release matrix tablet of Isoniazid was successfully formulated and evaluated. In the present study it was found that Isoniazid F3 and F4 formulation exhibited satisfactory results. It can be concluded from the present investigation that formulation of sustained release matrix tablet of Isoniazid with *Dioscorea mucilage* may become an ideal formulation for treatment of tuberculosis where unremitting supply of drug will be available for about 12 hrs. The yam polysaccharide may be established as best polysaccharide for the preparation of SR matrix products.

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