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ORIGINAL RESEARCH ARTICLE

Study of Binding Efficiency of Tapioca Starch using Iornoxicam as a Model Drug

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ABSTRACT

In the following study starch obtained from the Tapioca is a starch extracted from the root of the plant species *Manihot esculanta* was used as a binder in different concentrations in Lornoxicam tablets. The tablets were formed by wet granulation method by using 2% w/v, 4% w/v, 6% w/v, 8% w/v and 10% w/v tapioca starch as binding agent. Formulated Lornoxicam tablets were further evaluated for various parameters i.e. weight variation, hardness, friability,drug content, disintegration time and *in-vitro* drug release. The starch obtained from *Manihot esculanta* was found to have a good binding property. The hardness and disintegration time of the tablets was found to be increased with increase in starch concentration. Tablets with highest binder concentration showed maximum hardness (7.96 kg/m2) and disintegration time (28.10min) and minimum friability (0.1%). After one hour tablets with 2% w/v starch showed maximum drug release (97.05%) and tablets with 10% w/v starch showed minimum drug release (79.98%).

Key words: Starch, Tapioca, Binder, *In-vitro* dissolution, Lornoxicam

INTRODUCTION

Tapioca is a starch extracted from the root of the plant species *Manihot esculenta*. The name tapioca is derived from the word tipi'óka, the name for this starch in Tupi. This Tupi word refers to the process by which the starch is made edible. Tapioca is gluten free, and almost completely protein free.

Binders are pharmaceutical excipients that are commonly employed in tablet formulations to impact cohesion on the powder mix and hence improve on the flow properties of the granules. Binders act by causing aggregation of powders thereby forming granules through the process of granulation. They modify the cohesive properties of the granules by promoting the formation of strong cohesive bonds between such particles.

Tapioca Starch can be substituted for Potato Starch and Corn Starch. *Tapioca starch* does not contain any impurities to mask light flavors. It produces a clear film and gel and provides a lower viscosity while hot. As a high-quality starch, tapioca starch is characterized by a high water retention capacity.

In drug delivery systems, polymer plays a vital role. Development of new excipients is time consuming, involves tedious procedures and is highly expensive. Instead, identification of new uses for the existing substances is relatively inexpensive and less time consuming. Different synthetic binders (HPMC K4M, Sodium CMC,etc) are used in tablet formulation. But there has been ever increasing demand for the plant based products as excipients. Natural polymers have advantages over synthetic and semi-synthetic polymers like low cost, natural origin,less side effects, locally available and better patient tolerance. However, these natural substances suffer with the drawbacks like purity, source and microbial contamination. If these factors can be identified and controlled, natural substance can be good substitute for synthetic polymers. Natural polymers are used as binding agents, gelling agents, disintegrating agents, sustaining agents in matrix tablets, film forming agents, suspending and emulsifying agents for granule coating and microencapsulation.

Lornoxicam:

Lornoxicam is a member of the oxicam group of nonsteroidal antiinflammatory drugs (NSAIDs). Oxicams have potent antiinflammatory and analgesic effects. Lornoxicam is absorbed rapidly and almost completely from the gastro-intestinal

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tract. Maximum plasma concentrations are achieved after approximately 1 to 2 hours. Food protracts the average time to maximum concentration from 1.5 to about 2.3 hours and can reduce the area under the curve (AUC) by up to 20%. The absolute bioavailability of Lornoxicam is 90–100%. No first-pass effect was observed. 5'-HydroxyLornoxicam, the main metabolite of it.

Lornoxicam is found in the plasma in unchanged form and as its hydroxylated metabolite which exhibits no pharmacological activity. CYP2C9 has been shown to be the primary enzyme responsible for the biotransformation of the Lornoxicam. Approximately 1/2 to 2/3 is eliminated via the liver and 1/3 to 42% (data are inconsistent) via the kidneys as 5'-hydroxyLornoxicam.It has short biological half life (3-5 hrs)

The clinical trials published so far, mostly comparative, clearly document the efficacy of Lornoxicam as a potent analgesic with excellent anti-inflammatory properties in a range of painful and/or inflammatory conditions,including postoperative pain and rheumatoid arthritis. But their use is associated with a high risk of gastrointestinal adverse effects.

MATERIALS

In the present study the materials used were Lornoxicam, Tapioca starch, Potato starch, Lactose, magnesium stearate. The equipment used were tablet compression machine, UV visible spectrophotometer, dissolution test apparatus, disintegration test apparatus, electronic balance, hardness tester and friability test apparatus.

SIMPLE PROCESS FOR CASSAVA STARCH PRODUCTION:

Starch is the main constituent of cassava. About 25% starch may be obtained from mature, good quality tubers. About 60 % starch may be obtained from dry cassava chips and about 10 % dry pulp may be obtained per 100 kg of cassava roots.

1. Treatment of roots:

At first the roots were washed and carefully peeled off. The roots were then ground in a small blender to obtain the mash. The mash was washed on a sieve of 90 pm size. The residual fibre was dried. The sieve effluent was separated into solid and liquid fractions and the solid fraction was purified on a refining table. A fixed amount of water was added to rinse the precipitated starch on the refining table. The starch was collected and dried. The effluent was centrifuged to remove the solids. An aliquote of clear supernatant was freeze dried to determine the amount of soluble.

2. Treatment of chips and pellets:

The chips and pellets were ground in a pin mill. The starch was isolated from the material of particle size < 150 pm. For this purpose the chips were directly washed and they were also treated in two different ways before washing.

2.1 Processing of material without pretreatment:

The ground material was washed over a sieve of 90 pm. The residual fibre was dried and the sieve effluent was treated as described under 1. The starch left on the refining table was mixed with water again and was refined once more. The precipitated starch on the refining table was rinsed with a fixed amount of water. The starch and the solids of process water were dried. Moreover, an aliquote of the process water was freeze-dried to determine the total amount of soluble

2.2 Processing of material with pretreatment:

The material was stirred with 0.2% H_2SO_4, solution at 40 "C for 48 h as first way of pretreatment. In the second way of pretreatment the material was stirred for 48 h at 37°C in active fermenting fruit water, which was obtained from the fresh roots. During the fermentation lactic and acetic acid were produced. After the pretreatments, suspensions were treated as described in 2.1.

Fresh tubers are processed during season and dry chips during the off-season in some countries. For cassava, the process of starch extraction is relatively simple as there are only small amounts of secondary substances, such as protein, in the roots. When cassava roots are harvested or selected for starch extraction, age and root quality are critical factors. Cassava roots need to be processed almost immediately after harvest, as the roots are highly perishable and enzymatic processes accelerate deterioration within 1-2 days. A first-rate quality starch can be obtained from cassava using only water, and this makes the processing of cassava starch and flour particularly suitable for developing countries and rural industries.

EVALUATION OF TAPIOCA STARCH

Bulk and tapped density of starch:

Exactly 50 gm of starch powder was weighed on chemical balance and transferred into a 100 ml measuring cylinder. The cylinder was dropped on a wooden platform from a height of 2.5 cm three times at 2 second interval. The volume occupied by the starch recorded as the bulk volume. The cylinder was then tapped on the wooden platform until the volume occupied by the starch remained constant. This was repeated three times for starch powder. The data generated were used in

computing the Carr's index and Hauser's ratio for the starch.

Swelling power:

Starch was accurately weighed (2 g) into a dry tarred pre-weighed 250 ml centrifugal bottle. Distilled water was added to give a total volume of water equivalent to 180 g. The starch was completely suspended by stirring at 200 rpm using a magnetic stirrer. After taking out the stirrer, the bottle was immediately placed in a temperature-controlled water bath at 85 ±C 0.3with continuously shaking at 200 rpm for 30 minutes. The centrifugal bottle was then dried and placed on a balance followed by the addition of distilled water to bring to a total weight of 200 g. After capping, the bottle was centrifuged for 15 minutes at 1000g for 15 minutes. To measure solubility, 50 ml of the supernatant was then pipette and transferred into an evaporating petridish and dried overnight in a hot air oven at 105^{o}C. The dried residue was then cooled in desiccators and weighed for soluble starch. To measure the swelling power, the residual supernatant was carefully removed and discarded. The bottle with the sediment paste was then weighed to give the weight of swollen starch granules. The result was expressed by the calculation.

Gelling concentration of starch [5]:

Different concentrations of dry powder were mixed with distilled water by using laboratory stirrer and the gel forming concentrations were found out.

Measurement of diameter of starch grains [7]:

The diameter of starch grains was measured by using a eyepiece micrometer and a compound microscope. Powder was stained with N/20 iodine, mounted on a microscopic slide using lactophenol and the diameter of starch grains was calculated randomly.

Table 1: Evaluation of Tapioca Starch

Properties	Tapioca starch
Bulk density(g/cm^3)	0.52
Tapped density(g/cm^3)	0.71
Hausner's ratio	1.02
Carr's index	29.71
Swelling power	28.23
Diameter of starch grains (µm)	5.2-16.3
Gelling concentration(%w/v)	3-6
Total microbial load	Pass

Total Microbial Load of the Isolated Starch [8]:

The total microbial load is an important parameter, which decides the suitability of a substance for use as an excipient in pharmaceutical dosage form. According to many Pharmacopoeias, for synthetic and semisynthetic substances, the total aerobic count should not be more than 100 colonies forming unit (cfu) per gram, and the total fungal count (including yeast and moulds) should not exceed 50 cfu/g.

FORMULATION AND EVALUATION OF LORNOXICAM TABLETS

Formulation of Lornoxicam tablets

For the evaluation of the starch as binder, Lactose was used as a diluents in the prepared Lornoxicam tablet. The composition of tablet formulation containing Lornoxicam is given in (**Table 2**).

Table 2: formulations of tablet

Ingredients	T1	T2	T3	T4	T5	P4
Lornoxicam(mg)	10	10	10	10	10	10
Starch(%)	2	4	6	8	10	8
Lactose (mg)	89	89	89	89	89	89
Magnesium stearate (mg)	0.5	0.5	0.5	0.5	0.5	0.5
Total weight(mg)	100	100	100	100	100	100

Wet granulation and compression

Wet granulation method was used for all tablet production. The calculation is made for 30 tablets in each batch. In case accurately weighed quantities of each ingredient were mixed in a mortar and an appropriate quantity of the starch mucilage was added as a granulating agent and mixed for 20 min in a mortor. The damp mass was sieved with sieve no. 22 and dried at 50^{0}c oven for 6 hrs. The dried granular mass was passed through sieve no. 40 to obtain uniform sized granules. The different batches of the granules specified amount of were then mixed with calculated equal quantity of magnesium stearate (0.5%),, then compressed into tablets under constant pressure with a 8 station rotary tablet machine.

Tablets each containing 10 mg of Lornoxicam were also prepared employing Potato starch as per the formula given in Table 2. The procedure followed is as described above.

EVALUATION OF TABLETS

Hardness test:

Five tablets were selected at random from each batch to perform this test. Pfizer hardness tester was used to measure the hardness. Tablet was placed between spindle and anvil of the tester and the calibrated scale adjusted to zero, then applied a diametric compression force on the tablet and the position on the calibrated scale at which the tablet broke was recorded in Kg/cm². A mean hardness was calculated for each batch. The results are given in Table 3

Weight Uniformity test:

Twenty tablets from each batch were selected randomly and weight individually using a highly sensitive electronic balance. Their mean weights were calculated for each batch.

Friability test:

Ten tablets were selected at random, dusted and weighed together using electronic balance and then placed in the friabilator. The machine was operated for 4 min at 25 rotations per min and then stopped. The tablets were dusted and again reweighed. The percentage losses were calculated for each batch of the tablets.

$$\text{Percent Friability} = \frac{\text{Weight}_{final} - \text{Weight}_{original}}{\text{Weight}_{original}} \times 100$$

The results are given in (**Table 3**)

Uniformity of Drug Content:

Ten tablets were accurately weighed and powdered individually. Contents of each tablet were taken into ten separate 50 ml volumetric flask and 20 ml of methanol was added to each volumetric flask. The mixture was shaken thoroughly for about 30 min. These were kept in hot water bath to dissolve the Lornoxicam and the solution was made up to volume with methanol and mixed well, and then the solution was filtered through Whatmann filter paper No: 42. From the filtrate 1 ml was pipetted out and diluted with 10 ml of phosphate buffer of pH 7.4. The resulting solution from each sample was measured at 376 nm for the drug content. The results are given in Table 3

Disintegration time:

The method specified in the USP/NF (1980) was used. Disintegration medium used was 100 ml of 0.1 N HCl maintained at temperature between 35 and 39ºC throughout the experiment. Five tablets selected at random from each batch were placed one in each of the cylindrical tubes of the basket but no disc was used. The time taken for each tablet to break up into small particles and pass out through the mesh was recorded. Mean disintegration time was calculated for each batch.

Table 3: Weight, hardness, friability and drug content of lornoxicam tablets prepared employing tapioca starch Parameter

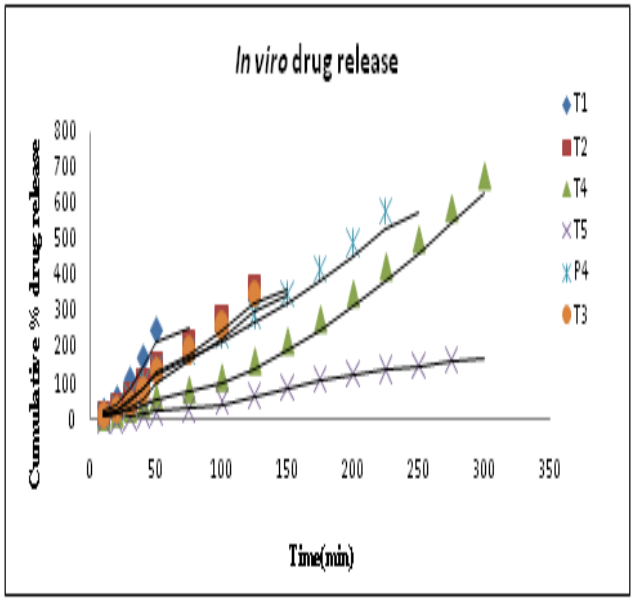
Parameter	T1	T2	T3	T4	T5	P4
Weight (mg)	99.35	99.85	99.95	99.1	100.05	99.35
Hardness(kg/cm^2)	2.86	4.1	4.7	5.9	7.96	5.4
Friability (%)	0.7	0.5	0.4	0.3	0.1	0.3
Drug content (%)	99.29	98.28	95.35	99.73	95.17	95.62
Disintegration Time(min)	18.50	21.30	22	25.58	28.10	27

***In vitro* release studies:**

Lornoxicam release from the tablets prepared was studied using 8 station dissolution rate test apparatus employing a USP-II (paddle) stirrer at 100 rpm and at37±0.5ºC. Phosphate buffer of pH 7.4 (900 ml) was used as dissolution fluid. Samples of 5 ml of each were withdrawn at different time intervals. Each sample withdrawn was replaced with an equal amount of fresh phosphate buffer pH 7.4. Samples were suitably diluted and measured at 376 nm for Lornoxicam using a Shimadzu UV-150 double beam UV Spectrophotometer. The results of *in vitro* release profiles obtained for all the formulations were fitted into four models of data treatment as follows:

1. zero-order kinetic model.
2. First- order kinetic model.
3. Higuchi's model.
4. Korsmeyer-Peppas equation.
5. Hixson Crowell model.

Fig 1: *In vitro* Drug release profile



RESULTS AND DISCUSSION

Table 1 shows the physical properties of Tapioca starch. The prepared tablets of lornoxicam with tapioca starch as binder were evaluated for parameters such as avg. weight variation, hardness, friability, disintegration, drug content are shown in table-3. Tapioca starch showed significant binding property. The average weight variation of the formulated tablets was found to be within acceptable limits. The hardness of the tablets increased with the increase in binder concentration. The friability was found to be decreased as the binder concentration increases. The disintegration time was found to be increased with the increasing concentration of tapioca starch.

Drug Release Kinetics: *In vitro* drug release data of all the formulations was subjected to goodness

of fit test by linear regression analysis according to zero order and first order kinetic equations, Higuchi's and Korsmeyer–Peppas and Hixson crowell models to ascertain the mechanism of drug release.

It can be observed from the results that tablets prepared using the tapioca starch as binder showed significant hardness and friability. Thus on the basis of the study it can be concluded that the starch obtained from *Manihot esculenta* possesses significant binding properties. So it can be used as tablet binder in pharmaceutical formulations.

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