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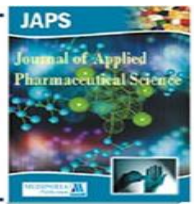


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# Formulation of Diclofenac Sodium tablets using Tapioca starch powder- A promising binder

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## ABSTRACT

Formulation research is oriented towards increasing safety and efficacy of existing drug molecule through novel concepts of drug delivery. Diclofenac is a semi-synthetic NSAID used as analgesic and anti-inflammatory. An attempt was made to identify the use of a natural product tapioca starch as binding agent in the formulation of Diclofenac tablets. To establish two other commonly used disintegrating agents potato starch and maize starch were selected and formulated for comparison. Different formulations were prepared by using above three disintegrants in the concentration of 20mg per tablet. The tablets were prepared by wet granulation technique. All the formulations were subjected to in in-vitro evaluation and the results were compared. The formulation containing tapioca starch powder showed good dissolution characteristics, within the Pharmacopoeial limits and comparative to potato and maize starch.

***Key words***: Diclofenac sodium, Tapioca Starch, Potato starch, Maize starch, M.C.C.P, PVP, Magnesium Stearate.

## INTRODUCTION

The nature and amount of the binders were found to alter the disintegration and dissolution rates of the tablets by reducing their wet ability as measured by the adhesion tension of water. During pharmaceutical granulation, the objective is to produce granules that have a uniform (and repeatable) distribution of drug particles within the bulk carrier (excipient) solid (Hapgood et al., 2002). This can be difficult to achieve and both drug depletion and enrichment in granules can occur (Zhang and Johnson, 1997). A linear relationship has been found to exist between the adhesion of water on the tablets and their disintegration and dissolution rates. Tapioca (*Manihot esculenta*) is also known as Cassava belongs to the Euphorbiaceae family. It is a woody shrub native to west Brazil. It is cultivated as an annual crop for its edible starchy tuberous root. The starch was extracted from the tuberous root of tapioca and used as human food, biofuel, animal feed and also in ethno medicine (Simons et al., 2004). However, the present study focuses on the starch extracted from tapioca used as binders in the Diclofenac sodium tablets and compared with the commercially available Maize starch and Potato starch for the dissolution properties.

## MATERIALS AND METHODS

The materials used were Diclofenac sodium (Accent Pharma, Puducherry), Maize Starch, Potato starch M.C.C.P, PVP, Talc, Magnesium Stearate, and Tapioca starch extracted from *Manihot esculenta* in our laboratory.

**Extraction of Tapioca Starch**

The starch was extracted from root tubers of cassava (*Manihot esculenta)* according to the method of Alebiowu (Alebiowu, 2007) using established procedures (Young et al.,1984). Cassava tubers were peeled, washed and cut to small pieces. These small pieces were then soaked in distilled water for specified period of time i.e. for 1 h. At the end of the steeping period, the softened tubers were milled to a pulp, and more distilled water was added to give dilute slurry which was sieved using mesh size 100 µ. This process was repeated three times until starch was fully extracted from the tubers as confirmed by iodine test on the remaining chaff, which were negative (Ring. 1985). The extracted starch was dried at 50$^{o}$C in a hot air oven for 72 h (Fu et al., 2004). The dried mass was powdered in a laboratory mill. The starch was then passed through a no. 120 mesh sieve and stored in an amber colored screw capped bottle before use.

**Granulation**

***Preparation of Starch Paste***

The weighed amount of starch was suspended for 10 min in distilled water in a beaker with continuous stirring to allow hydration before heating. The solution was used while still hot for more effective binding. It has been observed that during paste formation, not all of the starch is hydrolyzed.

**Preparation of PVP Solution**

A PVP solution was prepared by weighing the required amount of PVP granules that would produce a 4.0% w/w concentration of starch disintegrant in the formulation. Finally the PVP solution was poured into the starch solution and mixed well and the mixture is heated in a boiling water bath with continuous stirring until translucent paste forms (Bowen and Vadino 1984).

**Preparation of granules**

The wet granulation method of massing and screening was used. 300 gram batches of formulation mixtures of Diclofenac sodium, MCCP and starch (tapioca starch/ maize starch/ potato starch) were mixed. For small batches the ingredients may be mixed in stainless steel bowls or mortars. They were then moistened with PVP binder solution to yield 4% w/w PVP in the final dried granulation. The resulting wet masses were granulated by passing them manually through a 12 # mesh sieve, dried at 60$^{o}$C for 6 h, and then re-sieved through a 16 # mesh sieve. The dried granules were lubricated by using talc and magnesium stearate. Particle densities were determined using the pycnometer method with acetone as the displacement fluid.

**Preparation of tablets**

Quantities (250g) of granules from each batch were compressed into tablets with predetermined loads on a Pharma 100 multi-station rotary tablet press with a 10.5mm die and flat faced punch assembly. A set of tablets were produced from each pressure. After ejection, the tablets were stored in airtight containers to allow for elastic recovery and hardening, and prevent falsely low yield values before the tablets were subjected to analysis.

**Evaluation of tablets**

***Tablet Hardness***

The resistance of the tablet to chipping, abrasion or breakage under conditions of storage, transportation and handling before usage depends on its hardness (Lachman, 1991). Different types of Hardness tester were used as Strong Cobb, Monsanto, Pfizer and Scheluniger tester.

***Friability***

Measurement is made by use of the Roche friabilator. This instrument is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. A number of tablets were weighed and placed in the tumbling apparatus. After a given number of rotations of tablets were weighed and the loss in weight indicates the ability of the tablets to withstand this type of wear.

***Tablet thickness***

Tablet thickness was determined with a Caliper or thickness gauge which measured the thickness in millimeters. +5% or -5% may be allowed depends on the size of the tablet.

***Disintegration test***

Tablet disintegration time (DT) was determined in distilled water at 37 ± 0.5$^{O}$C in a disintegration test unit. The tablets were placed on the wire mesh just above the surface of the distilled water in the tube. The time taken for each tablet to disintegrate and all the granules to go through the wire mesh was recorded.

***Dissolution test***

The dissolution test was carried out by using the rotating basket method. The beaker is immersed in the water bath of temperature 37°C. It is filled with 900 ml of ($P^{H}$ 7.4) Phosphate buffer and the apparatus was set at 150 rpm. The samples were taken in the interval of 10 minutes and estimate the content by spectrophotometer at 276 nm. The same procedure was repeated at different time intervals and absorbance was noted and the percentage drug release was calculated.

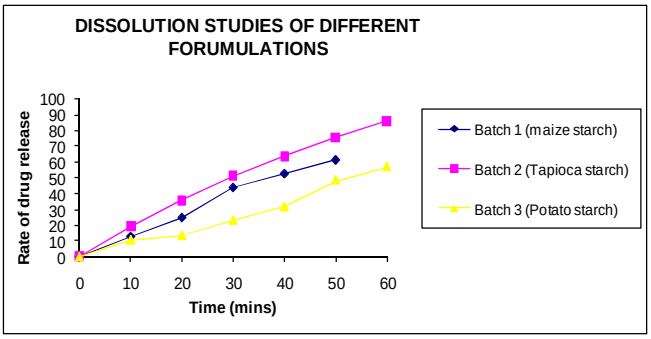


**Fig 1:** Dissolution studies.

## RESULTS AND DISCUSSION

The tablet manufactured by using Tapioca starch is better in friability and hardness than that of tablets made up of Maize starch and potato starch. Table 1 shows the effect of following physical properties - friability, hardness and disintegration time of the tablets prepared by different batches. As the disintegration time for the tablets formulated by using Tapioca starch has increased than that of industrial starch. It is concluded that the binding capacity of Tapioca starch would be many times greater than that of maize starch and potato starch. So if the concentration of Tapioca starch is decreased then the same effect may be obtained.

**Table 1: Physical properties (as per I.P)**

**Table 1: Physical properties (as per I.P)**

| Batches | Trial | Weight variation (%) | Friability (Friability in %) | Hardnes (In kg/ $cm^2$) | Disintegration time (In sec.) |
|---|---|---|---|---|---|
| I Maize starch | I | +4.5 ; -2.5 | 0.30 | 3.5 | 22 |
| | II | +5 ; -0.5 | 0.32 | 3.5 | 23 |
| | III | +4 ; -3 | 0.30 | 4.0 | 22 |
| II Tapioca starch | I | +5 ; -2 | 4.5 | 4.5 | 20 |
| | II | + 3 ; -1 | 5.0 | 5.0 | 22 |
| | III | +4.5 ; -1.5 | 4.5 | 4.5 | 20 |
| III Potato starch | I | +3.5 ; -4 | 0.32 | 3.0 | 23 |
| | II | +4 ; -2.5 | 0.28 | 3.5 | 25 |
| | III | +4.5 ; -3 | 0.28 | 3.5 | 23 |

From dissolution study of Diclofenac tablets formulated by using Tapioca starch has increased release of 21% than that of Maize starch represented in Table 2.

**. Table 2: Dissolution studies**

| Time (mins) | Batch 1 (Maize starch) | Batch 2 (Tapioca starch) | Batch 3 (Potato starch) |
|---|---|---|---|
| 10 | 12.8 | 19.3 | 10.6 |
| 20 | 24.7 | 35.6 | 13.5 |
| 30 | 36.2 | 51.4 | 22.9 |
| 40 | 43.9 | 63.8 | 31.7 |
| 50 | 52.7 | 74.6 | 48.4 |
| 60 | 60.3 | 87.2 | 56.9 |

## CONCLUSION

It has been concluded from the results in this study that the relative concentration of tapioca starch will have noticeable effects on the friability, hardness, disintegration time and percentage of drug release from the tablets produced. The percentage of drug release shows that the tapioca starch had a great influence on binding strength of the tablet which is shown in graph 1. If this could be proved in a large scale, then it is very much beneficial to the tablet manufacturing industry as it is cheap and abundantly available. Further study on this starch as a binder at different concentrations and with different drugs would give further information which is needed to establish the usefulness of this starch, as an effective binder in the field of tablet manufacturing.

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