International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.2, No.1, pp 406-411, Jan-Mar 2010

FORMULATION OF PARACETAMOL TABLETS USING A NOVEL BINDER ISOLATED FROM MANIHOT ESCULENTA.L AND ITS EVALUATION

V.CHALAPATHI[1]*, T.V.YUVARAJ[2]., A.JAGANATHAN[3]

[1]Department of Pharmacognosy, [2]Department of Pharmaceutics,

Mother Theresa Postgraduate and Research Institute of Health Sciences,

Puducherry, India - 605006.

[3]Accent Pharma, Puduchery, India

Corres Author: chalapathi03@gmail.com,
Mob: +919786577582.

Abstract: Pharmaceutical Manufacturing is an important enterprise and oral tablet Manufacturing is the most significant of all, because more drugs are made as tablets than any other dosage form. The way of tablet Manufacturing has been undergoing change in recent years and is likely to head in new directions. In this study Manihot esculenta (Maravalli kizhangu) a freely available & cheap starch has been chosen as a binder and studied for its effectiveness by comparing with the industrial Maize starch. As a consequence, the requirements for inert ingredients used in tablet Manufacture, in particular the requirements for tablet binders used in wet granulation, are undergoing change as well. A binder play a great role in the determination of disintegration time & dissolution of tablets, choosing of binder & disintegrators is also important.

Key Words: Paracetamol, Maize Starch, Gelatin, M.C.C.P, Magnesium Stearate, Lactose, Di Calcium Phosphate, disintegration test and dissolution test.

Introduction

Manihot esculenta L is commonly named as Cassada, Cassava, Manioc, Yuca, tapioca, Mandioca, Shushu, Muk shue, Assave, Maniok, Imanoka, Maniba, Kasaba, Katela boodin. In particular, this report describes a Preliminary exploration of the Potential of the roots of two local tubers Manihot esculenta Crantz and tapioka Manihot dulcis (J.F. Gemel) Pax (Euphorbiaceae) to serve as biocatalysts. The roots of M.esculenta and M. dulcis are valuable for their contemporary economic importance; both are tropical roots used widely in a large variety of traditional food preparations, especially in Brazilian northeast, Latin America, Africa, and Asia. In the process of the manufacture of the flour of M.dulcis, popularly known as Mandioca, several thousand liters of water called ‘‘Manipueira’’ are discarded[1]. Synonyms are Manihot utilissima, Manihot aipi[2]. Cassava is grown for its enlarged starch-filled tuberous roots. The peeled roots of the sweet variety are usually eaten cooked or baked. The root of the bitter variety is very poisonous when taken as raw one. Cooking destroys the hydro cyanic acid; the cooking water must be discarded. The effects of starch obtained from cassava (Manihot esculenta) on the disintegration & dissolution rates of paracetamol tablets. The properties of tapioca obtained from cassava (Manihot esculenta) have been evaluated. Its binding effect in tablets of paracetamol on the disintegration and
dissolution rates were compared with tablets prepared with polyvinylpyrrolidone and gelatin. 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, on average, a uniform (and repeatable) distribution of drug particles within the bulk carrier (excipient) solid. This can be difficult to achieve and both drug

depletion and enrichment in granules can occur[3]. A linear relationship has been found to exist between the adhesion of water on the tablets and their disintegration and dissolution rates. The mucilage of cassava starch extracted from Manihot utilissima tubers, which grow widely in West African countries, were evaluated as binders for lactose granulations. The extracted starch was compared with the commercially available Maize starch. The results showed that lactose granulations prepared with Cassava starch possessed higher physical properties than those of granulations prepared with Maize starch. The binding efficiency of Cassava starch Mucilage was found to be higher. Most of the reported studies in the literature tend to focus on the effects on drug/excipient distribution as a function of differences in primary particle size [4, 5]. The expression which correlates the crushing load to the intra granular porosity of a given granulation batch was derived. The crushing load, W, of a given lactose granulation is correlated to the friability of the respective granulations and the expression W = A * (A/F) X holds. The compactibilitys of a given lactose granulations batch was assessed using a newly-derived expression similar to that of Heckel, and a parameter indicative of granulation compactibility representing the yield value was determined[6]. Cassava starch Mucilage was found to produce lactose granulations of better compaction behavior. Binders are used to provide a free flowing powder from the mixture of tablet ingredients. So that the material will flow when used on a tablet machine. The binders also provide cohesiveness to the tablet. Too little binder will give flow problems and tablets, which do not maintain their integrity. Too much may affect the release of the drug from the tablet and which will cause excessive wear of punches and dies. Binders are used both as a solution and in a dry from depending on the other ingredients in the formulation and the method of preparation. Starch paste has historically been one of the most common granulating agents. Cornstarch and maize starch is widely used as binders. The concentration may vary from 10-20%.Starch paste is not only useful as a binder but also is used as a method to incorporate some ingredients inside the granule. Measurements of the granule friability, tablet strength and capping index of paracetamol wet granulated with these binders were found to be in line with this ranking. Rowe showed that selection between binder systems for a drug can be gauged simply from the surface polarity of the drug concerned[7]. In a previous study, a novel micromanipulator technique was employed to measure and, hence, differentiate, the interaction between binder solutions (HPMC and PVP, both concentrated at 4%) and Paracetamol crystals[8]. one of these, from Manihot esculenta, which provides an S-configured product, has been cloned and over-expressed for potential industrial application[9].

The challenge is to relate what is observed at the solid–solid, solid–liquid and solid–vessel interfaces to multi-particle granules that often have unknown structures and compositions, particularly in relation to binder distribution, and that are experiencing Complex shear conditions. Nevertheless, progress is being made in the fundamental understanding of such aspects as granule strength[10-12], deformation [13, 14] and attrition[15].

Materials and Methods

Materials:

Paracetamol (Micro labs Pharmaceuticals Ltd., Puducherry), Maize Starch, Gelatin,
M.C.C.P (Tristar Formulations Ltd., Puducherry), Magnesium Stearate, Lactose, Di calcium Phosphate (Caplein Point Laboratories, Puducherry).

Methods:

Isolation of Starch from Manihot esculenta:

Wash potatoes thoroughly with water to remove adhering soil and earthy matter and reduce to fine slurry with water in a blender. Pass the slurry through shaking sieves in order to remove the cell debris and other impurities. Allow the milky liquid to settle down. Decant the supernatant liquid. Wash the starch 2-3 times with distilled water with constant stirring. Centrifuge the milky liquid, dry it in oven at a low temperature and powdered.

Preparation of Paracetamol Tablets Using Manihot esculenta Starch as Binder:

Sieving and Weighing of the ingredients. Weights of the ingredients were used as
Paracetamol, Starch (Manihot esculenta), Gelatin, Sodium benzoate, Micro Crystalline Cellulose powder and Magnesium stearate.

Granulation:

Preparation of Starch Paste:

Preparation of Starch solution:

16.2 gms of starch was taken in a beaker and 24ml of hot water was added and stirred well to make suspension and heated in a boiling water bath with continuous stirring until a translucent paste is formed. It has been observed that during paste formation, not all of the starch is hydrolyzed.

Preparation of Gelatin solution:

Gelatin solution should be freshly prepared and used while hot. 4 gms of gelatin was taken in a beaker and 16ml of boiling water was added and stirred well to form a solution by heating in a boiling water bath. Finally the gelatin solution was poured into the starch solution and mixed well and the mixture is heated in boiling water bath with continuous stirring until a translucent paste forms.

Wet Granulation:

The steps involved in wet granulation were, Weighing, Mixing, Granulation, Screening the damp mass, Drying, Dry screening, Lubrication and Compression.

The active ingredients of Paracetamol, diluents and disintegrants were mixed. For small batches the ingredients may be mixed in stainless steel bowls or mortars. A solution of the binding agents was added to the mixed powders with stirring. The powder mass is wetted with the binding solution until the mass has the consistency of damp snow. If the granulation is over wetted the granules will be hard, requiring considerable pressure to form the tablets. If the powder mixture is not wetted sufficiently the resulting granules will be too soft, breaking down during lubrication and causing difficulty during compression. The wet granulation is forced through a 6 or 8 mesh screen. The moist materials was placed on large sheets of paper on shallow wire trays and placed in drying cabinets with a circulating air current and thermostatic heat control. Particle size distribution can be controlled by varying the speed of rotation and drying temperature. After drying, the granulation is reduced in particle size by passing it through a smaller mesh screen. After dry granulation the lubricants such as M.C.C.P and Magnesium stearate was added. Then the lubricated granules were compressed by using Single punch Machine[16].

Preparation of Paracetamol Tablets by Using Maize Starch:

The ingredients were weighed as Starch, Sodium benzoate, Gelatin, Paracetamol, Starch (Maize starch), M.C.C.P, Magnesium stearate in the required quantities. Paracetamol Tablets by Using Maize Starch was prepared by same Procedure as Previously Mentioned.

Evaluation of Paracetamol Tablets Prepared by Using Above Mentioned Binders:

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. Different types of Hardness tester were used as Strong Cobb, Monsanto, Pfizer and Scheluniger.

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.

Tablet Weight:

The volumetric fill of the die cavity determines the weight of the compressed tablet.

The weight of the tablet is the quantity of the granulation which contains the labeled amount of the therapeutic ingredient. Twenty tablets were weighed individually and average weight was calculated. The variation from the average weight in the weights of not more than two tablets must not differ by more than the percentage.

Tablet Disintegration:

The apparatus consists of a basket rack holding six plastic tubes open at the top and bottom. The bottom of the tube is covered with 10 mesh screen. The basket rack is immersed in a bath of suitable liquid held at 37°C preferably in 1 litre beaker. The rack moves up and down in the fluid at specific rate. The end point of the test is indicated when any residue remaining in a soft mass having no probably soft core.

Results and Discussion

In this present study, paracetamol tablet were formulated using Manihot esculenta starch and industrial starch as a binder. The tablets were evaluated for, Physical Characteristics**,** Weight variation**,** Friability, Hardness, Disintegration test and Dissolution Studies.

Physical Characterists:

The Paracetamol tablets manufactured by using both Manihot esculenta a starch & industrial starch was found to be white, smooth and circular in appearance. They had sufficient hardness to withstand the wear & tear during the handling of the tablets for the various evaluation studies. The physical appearance of the tablets was same for both formulated as well as industrial starch.

Weight Variation:

The percentage weight variation of the tablet formulated from the Manihot esculenta starch was found to be 2.431 and that of industrial starch was 3.06% are given in table-1.

Batch 1 (Paracetamol Tablets By Using Industrial Starch as Binder).

Batch 2(Paracetamol Tablets by Using Manihot Esculanta.L Starch as Binder).

Friability:

The friability for tablets formulated using Manihot esculenta starch was found to be 0.1% which is 0.2% lesser than that of tablet formulated from industrial starch (0.3%) are given in table-2.

Hardness:

The hardness of the tablet formulated from Manihot esculenta starch was found to be 4—5 kg/cm^2 and that of industrial starch was 3-4kg/cm^2 are given in table-3.

Disintegration:

The disintegration time of the tablet formulated from the Manihot esculenta starch was found to be 20 mins and the disintegration time of the tablet formulated from the industrial starch was 22 secs are given in table-4.

Table-1. Weight Variations of Batch 1 and 2.

Sl.No.	Batch 1 (weights in mg)			Batch 2 (weights in mg)		
	I	II	III	I	II	III
1	252	264	270	262	252	265
2	260	256	263	264	260	260
3	270	248	265	270	270	250
4	263	250	252	265	263	263
5	265	255	260	267	265	268
6	255	250	268	250	255	270
7	268	252	270	255	268	250
8	270	260	248	248	270	248
9	270	265	250	250	270	255
10	265	270	255	263	265	270
11	264	252	260	260	255	273
12	256	260	265	265	250	270
13	248	270	263	258	248	260
14	250	263	264	255	256	260
15	255	265	270	260	264	255
16	250	255	262	265	250	261
17	252	268	260	263	252	263
18	260	270	265	250	260	265
19	265	270	250	255	265	260
20	270	265	255	260	270	255

Table-2. Friability of Batch 1 and 2.

Batch 1(Friability in %)			Batch 2 (Friability in %)		
I	II	III	I	II	III
0.30	0.32	0.30	0.15	0.10	0.10

Table-3.Hardness test of Batch 1 and 2.

Batch 1 (In kg/cm^2)			Batch 2 (In kg/cm^2)		
I	II	III	I	II	III
3.5	3.5	4.0	4.5	5.0	4.5

Table-4.Disintegration time of Batch 1 and 2.

Batch 1 (time in seconds)			Batch 2 (Time in minutes)		
I	II	III	I	II	III
22	23	22	20	22	20

Dissolution Study:

The characteristics of paracetamol tablet formulated from the Manihot esculenta starch and the tablet formulated from industrial starch were investigated adopting the USP XXII rotating basket apparatus at stirring rates of 100 rpm and a temperature of 37°C, 900 ml of distilled water utilized. The samples of 10 ml were withdrawn and measured spectro photometrically at 257nm by UV Spectrometer (Shimadzu). Dissolution Study of Batch 1 and 2 are given in table-5.

Conclusion

From the above result it is learn that the paracetamol tablet manufactured by using Manihot esculenta starch is better in friability and hardness than that of tablets made up of industrial starch (Maize). As the disintegration time for paracetamol tablets formulated by using Manihot esculenta starch has increased 60 times than that of industrial starch. It is concluded that the binding capacity of Manihot esculenta starch would be many times greater than that of industrial starch. So if the concentration of Manihot esculenta starch is decreased then the same effect may be

obtained. From dissolution study paracetamol tablets formulated by using Manihot esculenta starch has increased release of 21% than that of industrial starch. If this could be proved, 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.

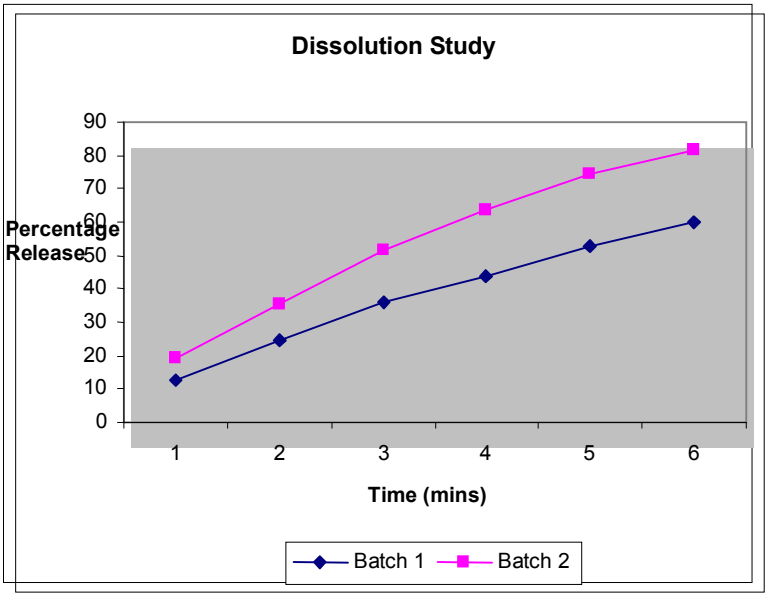

Fig -1. Dissolution Study of Batch 1 and 2.

Table -5.Dissolution Study of Batch 1 and 2 in D60 mins.

Time (mins)	Batch 1(%)	Batch 2(%)
10	12.8	19.3
20	24.7	35.6
30	36.2	51.4
40	43.9	63.8
50	52.7	74.6
60	60.3	81.5

References

1. Braga, R., Plantas do Nordeste: Especialmente do Ceara, Colecao Mossoroense, Natal, RN, Brasil, 1976,4Ed, 330- 343.
2. Gunapadam.P.N., Murugesa Mudhaliar K.S., 1951,67.
3. Hapgood, K., Hartman, H.E., Kaur, C., Plank, R., Harmon, P., Zega, J.A., Proceedings of the World Congress of Particle Technology, 2002, 4, 21–25.
4. Zhang. Y., Johnson K.C., Int. J. Pharm. 1997, 154, 179–183.
5. Vromans.H. Poels-Jansseen H.G.M., Egermann H., Pharm. Dev.Technol.1999, 4, 297– 303.
6. Remington, Science and practice of Pharmacy, 2002, 1,894-902.
7. Rowe R.C., Int. J. Pharm. 1989, 56, 117– 124.
8. Simons, S.J.R., Rossetti, D., Pagliai, P., Ward. R., Fitzpatrick.S. Powder Technology 2004,140, 280–289
9. Johnson, D.V., Griengl.H. Biocatalytic applications of hydroxynitrile lyases. Adv. Biochem. Eng/Biotechnol. 1999, 63, 31–55.
10. Ennis B.J., Jinlang L., Tardos G.I., Pfeffer R., Chem. Eng. Sci. 1990, 45,3071– 3088.
11. Pepin X., Simons S.J.R., Blanchon .S. Rossetti .D. Couarraze.G. Powder Technol., 2001, 117, 123– 138.
12. Iveson S.M., Beathe J.A., Page N.W., Powder Technol. 2002, 127,149–161.

13. Fu J., Adams M.J., Reynolds G.K., Salman A.D., Hounslow M.J.,Impact deformation and rebound of wet granules, Powder Technol., 2004, 140, 248– 257.
14. Lian G., Thornton C., Adams M.J., Thornton .C. (Ed.), Powders and Grains, Balkema, 1993.
15. Samimi A., Ghadiri M., Boerefin R., Kohlus R., Proc. 7th Int. Sym. Agglom., paper Albi, France,2001,113, 29– 31.
16. Lachman, Lieberman, Kanig, The theory and practice of industrial Pharmacy, 1991, 4 Ed, 293-333.

*****