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Original Article

Binding Properties of Ethyl Starch obtained from *Ipomoea batatas* as a Pharmaceutical Excipient

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ABSTRACT

The aim of the study was to extract, modify and evaluate the binding efficacy of starch obtained from sweet potato in paracetamol tablet formulation. Starch, in its native state, exhibits limited applications due to low shear stress resistance and thermal decomposition, high retrogradation and syneresis, therefore to meet the demanding technological needs, the properties of starch are modified by a variety of modification methods. Extracted starch obtained from sweet potato was modified using diethyl sulphate to obtain ethyl starch. The degree of substitution (DS) for the ethyl starch was determined, and the FT-IR analysis of both the native and the ethyl starch was carried out. The ethyl starch and the native starch were subjected to various material, and physicochemical property evaluations and the result were compared. Paracetamol tablets were formulated using native starch, ethyl starch and starch BP ® as binders at different concentrations and subsequently evaluated and compared using standard pharmacopeia procedures. DS of 0.728 was obtained, and evidence of OH substitution was confirmed as seen in the FTIR spectra. The ethyl starch was found to have better flow properties than the native because of its higher bulk, tapped and true densities, flow rate and lower angle of repose than that of the naïve starch. The ethyl starch shows higher swelling capacity (25.5) as compared to the native starch (10.5). Native starch showed good hardness properties as compared to ethyl starch and starch BP but with higher disintegration time. In conclusion, ethyl starch has less binding properties than native starch and starch BP but has improved material properties, higher purity and lower disintegration time.

Keywords: Sweet potato, Ethyl starch, Binding properties, Degree of substitution.

1. INTRODUCTION

Starch is a polysaccharide, widely used as binder, diluent, glidant and disintegrating agent in oral solid dosage formulation and also dusting powder and lubricant. Commercially starch is available from maize *(Zea mays*), potato (*Solanum tuberosum*), rice (*Oryza sativa*), tapico (*Manihot utilissima*) and wheat (*Triticum aestivum*) [1, 2]. Many scientists working on various sources of starch and

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modified forms, so provide and establish a binder that will be more useful in pharmaceutical manufacturing. Hence, the search for new starch is a continuous ongoing process worldwide. Starch is the most commonly used excipient in the pharmaceutical industry due to its interesting physical properties – e.g. disintegration and binding properties [3]. The use of starch is however limited by its poor flow property, compressibility and compatibility. Several modifications have been shown to improve those functional properties [4]. Modified starches, also called starch derivatives, are prepared by physically, enzymatically or chemically treating native starch, thereby change properties of the starch. The various types of modifications include heat gelatinization, enzymatic hydrolysis, acid hydrolysis and other various forms of chemical modification [5]. In this manuscript, we reported the isolation and ethylation of starch from *Ipomoea batata* and its use as an alternative binder to native and maize starch following an evaluation study of the formulated tablets.

2. MATERIALS AND METHODS

The root tubers of *Ipomoea batatas* were obtained from Kasuwan Daji, Sokoto state, Nigeria. All other chemicals and reagents used were of analytical grade.

Extraction

The procedure described by Alves *et al*.[6] was adopted with little modification. The tubers were peeled and cut into cubes. These cubes were then soaked in 10 liters 0.075 % of sodium meta bisulphite solution overnight. This mixture then milled, stirred and filtered using double-fold cleans cheesecloth which were allowed to settle whiles the starch sediments completely. This was followed by decanting the water and centrifuging the suspension at 4000 rpm for 10 min using Lab centrifuge (Thermo electron co. IEC FL40R, France). After centrifugation, the starch separated from water and non-water soluble constituents. Finally, the pure starch obtained from centrifugation air dried in a hot air oven and ground with a grinder (Super Master Co. Ltd. SMB-3377) and sifted through standard sieves. The flour was packed into an airtight container and stored at room temperature for further analysis

Starch Modification.

The procedure (organic slurry method of modification) described by lawal *et al.* [7] was used. To the native starch (50g), 200 ml of 0.1M NaOH was added and stirred until slurry formed. It was allowed to stay for 1hr in a water bath at a temperature of 40^0C. Excess NaOH was filtered, and then 5 ml of diethyl sulphate and 20 ml of acetone was added. The mixture was shaken for 1hr in a closed system at temperature of 40^0C with the pH adjusted to 5 by adding 10 % glacial acetic acid. After the reaction, it was filtered using filter paper and washed three times with acetone until the pH of the liquid is neutral. The modified starch was dried in an oven at a temperature of 45^0C for 6hrs. The dried ethyl starch was passed through a 100-mesh sieve.

Determination of Degree of substitution

The ethyl starch (0.5g) was dissolved in 20 ml of 0.1M NaOH, and 80 ml of distilled water was added, 25ml of the solution was transferred to an entrepreneur's flask and diluted by the addition of 75ml of distilled water. The excess of the NaOH was back titrated with standard 0.2M HCl using phenolphthalein as an indicator. The titration was repeated three times, and the average volume of HCL used was taking. A blank titration was also carried out. The DS was calculated using the standard method [8].

A=BC-DE/F

DS = (0.162) x A / 1- (0.031 x A)

Where

DS=Degree of substitution

A=Milimitre equivalents of consumed acid per gram of specimen

B=Milliliter of added NaOH

D=Milliliter of consumed HCL

E=Normal HCL

F= Specimen gram Used

162=Molecular weight of anhydrous glucose unit

58= Net increase in the anhydrous glucose unit for every substituted ethoxy group substituted

Assessment of Materials Properties

Bulk and Tapped Densities

The native starch (10g) was transferred into a clean and dry measuring cylinder and the volume (V) occupied by the sample without tapping was determined. Also, the volume (V) after 500 manuals tapping was determined. The bulk and tapped densities were determined as the ratio of the mass of the sample to volume. The procedure was repeated three times, and the average was used.

The above procedure was also repeated using ethyl starch. Carr's index and Hausner ratio were determined from the bulk and tapped density measurements.

True Density (Dt)

This was determined using the method (liquid displacement method described by Ohwoauvorhua *et al*. [9], using xylene as the immersion fluid.

D_t= W/[(a+w)-b] x SG

Where W= weight of sample S.G= Specific gravity of liquid (xylene), a=weight of bottle +liquid, b=weight of bottle +liquid=sample.

The angle of Repose and Flow Rate

The native starch (10g) was placed in a funnel which was clamped on a retort stand, the tip of the funnel was plugged with cotton wool. The cotton wool was later removed and the time taking by the powder to completely flow through the funnel was used to determine the flow rate as a ratio of mass of sample to time. Also, the height and the diameter formed by the powder were used to determine the angle of repose. This was repeated 3 times, and the average was used. The procedure was repeated using the ethyl starch.

Powder Porosity

It was determined according to the method of ohwoauvorhua *et al*. [9] using the equation

$e = 1-B_b/D_t \times 10$.

Where Bb=bulk density, Dt, true density e=porosity

Hydration capacity

The method described by Konbulum and stoopak [10] was used. A sample (1g) of the native starch was placed in each of three 15ml plastic centrifuge, and 10ml distilled water was added and mixed for 2 minutes on a vortex mixer. The mixture was allowed to stand for 10 minutes and immediately centrifuged. The supernatant carefully decanted, and the sediment was weighed. The hydration capacity was taken as the ratio of the weight of the sediment to the dry sample weight.

Swelling Capacity

This was determined at the same time as the hydration capacity determination and computed according to the following equation;

$S = (V_2-V_1)/V_1 \times 100\%$

Where S is the % swelling capacity, V_2 is the volume of the hydration or swollen material and V_1 is the tapped volume of the material before hydration.

Determination pH

A 2 g quantity of the powder material with 100 ml of distilled water was mixed for 5 min, and the pH of the supernatant liquid was determined using a pH meter (3510 model, Jenway, England).

Moisture Absorption

The native starch (2g) was placed into a crucible and the weight of the sample plus the crucible was determined. It was transferred into a desiccator in which water i.e relative humidity 100 % (400ml) was placed into the desiccator. It was weighed every day (for 5 days) and the gained in weight for each day was determined.The procedure was repeated using the ethyl starch.

FT-IR Analysis

Starch sample (50mg) was blended with solid KBr, (Merck, Germany) and about 40mg of the blended sample was used to prepare a pellet- (Hydraulic pellet press Kp, Mumbai, India). The spectra were scanned from 4500-250cm-1 in a PerkinElmer FT-1R spectrometer (PerkinElmer, USA) under dry air at 100m temperature.

Proximate and Elemental Analysis

The proximate analysis for moisture, crude protein, crude lipid, fibre and ash content of the native starch and modified starches obtained from *Ipomoea batatas* were carried out according to the method of the AOAC [11]. The conversion factor of total nitrogen to crude protein was 6.25. Percentage total carbohydrate was determined by subtracting the total of ash, crude protein, lipid and fiber from 100. The elemental analysis was carried out according to AOAC [11], and the following elements were determined; sodium, potassium, phosphorous, magnesium and calcium.

Granulation and Tableting

Wet granulation method was used to form the granules, and a single punch tableting machine was used in formulating paracetamol tablet each weighing 300mg. The table below (Table 1.0) summarized the formula used for the preparation of the tablets.

Evaluation of the Tablets

Uniformity of Weight Test

Twenty tablets were randomly selected from each batch. Individual weight of each tablet was determined, and then weight of all the sample tablets was also determined together. The percentage deviation was then calculated.

Hardness Test

Ten tablets from each batch were randomly selected and placed between the spindle of the Erwecka hardness tester machine and pressure was applied by turning knueled knot just sufficient to hold the tablet in position. The pressure was uniformly increased until the tablets breaks and the pressure was then recorded.

Friability Test:

Sample tablets (10 tablets) were randomly selected from each batch and weighed on the analytical balance. The tablets were then put in an automated friabilator spin at 100rev/ 4minutes to roll and fall within the rotating apparatus. After spinning, the tablets were reweighed after all the loose particles were dusted by gently blowing.

Disintegration Test:

Sample tablets (6 tablets) were randomly selected from each batch and the time for the disintegration of the tablets was determined at 37^0C in distilled water using a disintegration tester apparatus. And the time in which no granule of any tablet remained on the mesh was taking as the disintegration time.

Assay of the Tablet

A samples of 20 tablets were weighed and powdered.50 ml of 0.1M NaOH, and 25ml of distilled water was added slowly to a quantity containing 0.2g of paracetamol, shaked for 15mins and sufficient water was added to produced 100ml,mixed,filtered,10ml of the filtrate was made up to 100ml with distilled water,10ml of the resulting solution was added to 10ml of 0.1M NaOH diluted to 100ml with distilled water and the absorbance of the resulting solution was measured at 245 nm wavelength.

Dissolution Test

A dissolution medium of 900ml of 0.1M HCl solution maintained at 37^0C± 0.5 with a basket revolution of 25rpm was used. A 5ml volume of leaching fluid was withdrawn at intervals of 10,20,30,40,50 and 60 mins and replaced with an equivalent volume.1ml from the 5ml withdrawn was diluted with 9ml of distilled water and made up to 10ml. The absorbance of the resulting solution was measured at a wavelength of 245nm. The procedure was repeated using one tablet from each batch.

3. RESULTS AND DISCUSSION

The Degree of substitution was found to be 0.72 which indicated that substitution of OH group with ethyl took place evident From the FTIR result which showed the presence of an absorption peak band at 1200nm in the FTIR spectrum of ethyl starch (Fig. 3.0) which is absent in that of the native starch (Fig. 2.0). The ethyl starch had higher true, bulk and tapped densities (2.020, 0.577 and 0.683 respectively) when compared with the values of native starch(1.932,0.526 and 0.571 respectively). The native starch has lower Carr's index and Hausner's ratio than that of the ethyl starch. The ethyl starch has an angle of repose, which gives good flow (25.96) than that of the native starch (39.76). Therefore the ethyl starch is expected to have better flow than the native starch.

The ethyl starch also has higher hydration capacity than the native starch; it may be due to the addition of negatively charged ethyl group. Also, ethyl starch shows greater swelling capacity than the native starch, which is an index of good disintegrating property. Increase in swelling capacity of ethyl starch over native starch could enhance it disintegrating activity as it could lead to absorption of moisture absorption of large quantities of water and subsequent generation of higher swelling force [12]. The pH of the ethyl starch derivative (6.5) was slightly acidic than the pH value (6.8) recorded for the native starch. The ethyl starch shows greater moisture absorption than the native starch as shown in Fig.1, it may be due to the addition of negatively charged ethyl group.

The proximate analysis is a determinant of starch purity. Both the native and ethyl starch have moisture content <15%, which is the upper limit recommended by British pharmacopoeia, 2007. But the ethyl starch has a moisture content greater than that of the native starch. High moisture content could have adverse effects on its quality. Optimal level of moisture in starch (5-10%) have been shown to be essential in producing compact with high tensile strength and low friability(Aulton,2001). The ethyl starch have higher ash content than the native starch though it is greater than 0.6%in both which is the upper limit recommended by B.P. Low protein starch content(<0.2%) is recommended [13] as high protein content can influence their functional properties and result in false characterization [14]. Carbohydrate is an indirect measure of purity. The difference between carbohydrate content of the ethyl starch and the native starch is less significant (96.54 and 96.43 respectively).A good starch for pharmaceutical application should contain more than 96%w/w starch and as much as possible devoid of other plant components such as fiber, protein and lipid [14]. And all are less in the ethylated starch than in the native starch as shown in table 3, therefore the ethyl starch can be considered to be purer than the native starch.

Presence of inorganic salts and ions of phosphorus, iodine and OH group have been reported to contribute to starch granules swelling and gelatinization [13]. The native starch have a higher content of the sodium, potassium, magnesium and phosphorous than that of ethyl starch. Therefore it is expected to show greater granules swelling and gelatinization.

The ethyl starch also has lower hydration capacity than the native starch. Also ethyl starch shows greater swelling capacity than the native starch, which is an index of good disintegrating property. As per the physical characterization of the batch, from F1 to F13 do not show much difference in micrometric studies and granule flow property. The values ranged within the specified limits of good flow properties. The improve in the flow properties of the native starch is due to the formation of the granules as a result of increased in powder density, which allows smooth tablet compression [15]. For the weight variation test, all the batches passed the test because they have %deviation <7.5% which is the upper limit specified by United States pharmacopeia. From Table 7, the result shows that native starch had good crushing strength as compared to others; all batches had poor friability except batched with binder concentrations of about 10 %. Disintegration time of less than 15 min was recorded for all batches and also, the assay content of paracetamol in all batches was within the official specification of 90 – 110%. For the dissolution profile, all batches hard drug release profile greater than 80 % of the active content within 45 min as specified by the official compendia.

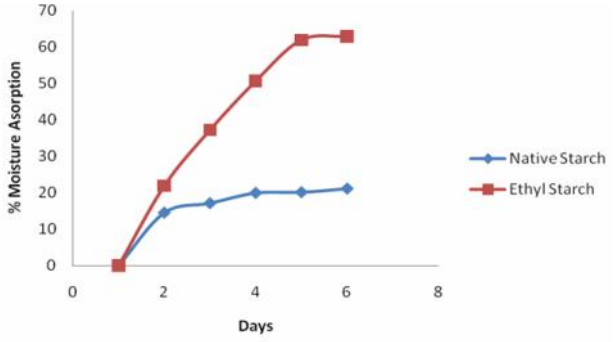

Fig 1: Moisture Absorption of Native and Ethyl Starch Obtained from Sweet Potato

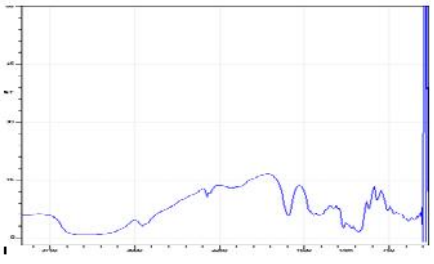

Fig 2 : FT IR Spectrum of Native Starch obtained from Sweet Potato

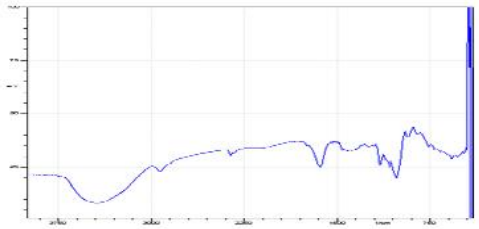

Fig 3: FT-IR Spectrum of Ethyl Starch obtained from Sweet Potato

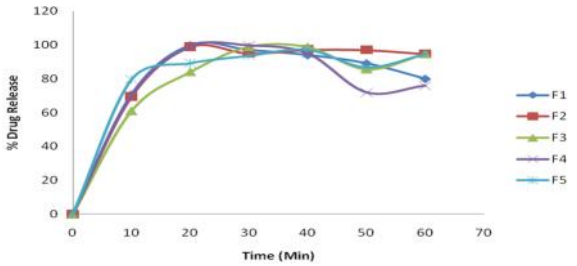

Fig 4 : Dissolution Test for Tablet Formulated using Native Starch as Binder

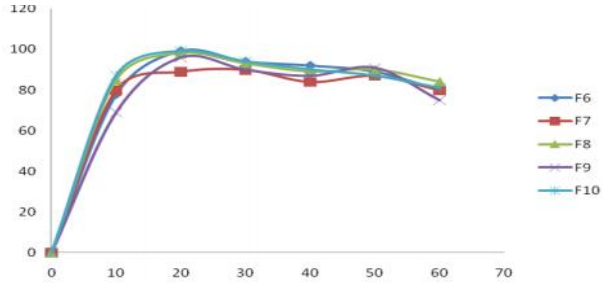

Fig 5: Dissolution Test for Paracetamol Tablet Formulated using Ethyl Starch as Binder

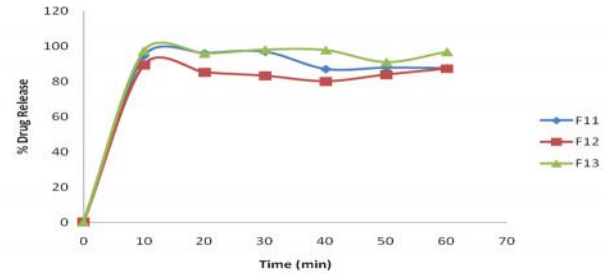

Fig 6: Dissolution Test for Paracetamol Tablet Formulated using Standard Starch as Binder

Table 1: Formula For Paracetamol Tablet Formulation

Batches	Paracetamol (mg)	Lactose (mg)	Maize Starch BP (I.D) mg	Starch Binder (mg)	Maize Starch BP (E.D) mg	Talc (mg)	Mg. Stearate (mg)
F1	200.00	64.90	7.50	6.00	15.00	6.00	0.60
F2	200.00	58.90	7.50	12.00	15.00	6.00	0.60
F3	200.00	52.90	7.50	18.00	15.00	6.00	0.60
F4	200.00	46.90	7.50	24.00	15.00	6.00	0.60
F5	200.00	40.90	7.50	30.00	15.00	6.00	0.60
F6	200.00	64.90	7.50	6.00	15.00	6.00	0.60
F7	200.00	58.90	7.50	12.00	15.00	6.00	0.60
F8	200.00	52.90	7.50	18.00	15.00	6.00	0.60
F9	200.00	46.90	7.50	24.00	15.00	6.00	0.60
F10	200.00	40.90	7.50	30.00	15.00	6.00	0.60
F11	200.00	55.90	7.50	15.00	15.00	6.00	0.60
F12	200.00	40.90	7.50	24.00	15.00	6.00	0.60
F13	200.00	25.90	7.50	39.00	15.00	6.00	0.60

KEY: I.D=Internal Disintegrant E.D=External Disintegrant F1-F5=Native Starch as Binder F6-F10=Ethyl Starch as Binder , F11-F13=Standard Starch BP

Table 2: Assessment of Material Property of Native and Ethyl Starch

Parameters	Native Starch	Ethyl Starch
Degree of Sub	-	0.728
Bulk Density (g/ml)	0.526±0.65	0.576±0.44
Tapped Density (g/ml)	0.570±0.44	0.682±0.36
Angle of Repose (^{0})	39.760±0.06	25.960±0.32
Flow Rate (g/s)	0.054±0.11	0.132±0..76
Carrs Index	7.828	15.555
Hausners Ratio	1.085	1.184
True Density (g/ml)	1.933±0.09	2.020±0.08
Powder Porosity	2.451±0.07	2.096±0.67
Hydration Capacity (%)	1.584±0.17	1.549±0.02
Swelling Capacity (%)	10.500±0.43	25.520±0.03
pH	6.800	6.500

Table 3: Proximate Analysis of Native and Ethyl Starch obtained from Sweet Potato

Analysis	Native Starch	Ethyl Starch
Moisture Content	1.600	1.800
Ash Value	1.000	1.2
Lipid	Trace	Trace
Fiber	Trace	Trace
Nitrogen	0.084	0.030
Crude Protein	0.930	0.237
Carbohydrate	96.386	96.733

Table 4: Elemental Analysis of Native and Ethyl Starch obtained from Sweet Potato

Element Content	Native Starch (mg/kg)	Ethyl Starch (mg/kg)
Sodium (Na)	15.00	10.00
Potassium (K)	25.00	22.50
Calcium (Ca)	1.15	1.15
Magnesium (Mg)	0.40	0.35
Phosphorous (P)	2.78	2.67

Table 5: Evaluation of Granules formulated using Native, Ethyl and Standard Starches

Batches	Bulk Density (g/ml)	Tapped Density (g/ml)	Carrs Index	Hausners Ratio	Angle of Repose (^{0})	Flow Rate (g/s)
F1	0.560±0.02	0.645±0.09	13.178	1.152	22.830±0.09	0.038±0.50
F2	0.510±0.01	0.625±0.05	18.400	1.225	18.500±0.70	0.154±0.88
F3	0.530±0.41	0.617±0.07	14.100	1.164	21.250±0.91	0.313±0.71
F4	0.560±0.31	0.625±0.14	10.400	1.116	22.090±0.07	0.204±0.84
F5	0.530±0.53	0.606±0.04	12.541	1.143	23.530±0.22	0.370±0.24
F6	0.416±0.01	0.500±0.89	16.800	1.201	25.910±0.17	1.110±0.42
F7	0.434±0.04	0.556±0.09	21.942	1.281	23.300±0.19	0.333±0.31
F8	0.476±0.01	0.625±0.61	30.560	1.313	27.700±0.29	0.294±0.43
F9	0.476±0.60	0.556±1.70	14.388	1.222	16.110±0.08	0.909±0.81
F10	0.455±0.40	0.588±0.80	22.619	1.292	23.700±0.77	0.227±0.12
F11	0.440±0.23	0.576±0.55	23.611	1.309	17.450±0.65	0.370±0.25
F12	0.450±0..15	0.556±0.04	19.064	1.311	20.650±0.52	0.714±0.33
F13	0.480±0.43	0.585±0.29	17.949	1.290	18.430±0.75	0.556±0.01

Table 6: Evaluation of Tablets formulated using Native, Ethyl and Standard Starches

Batches	Hardness (kg)	Friabilty (%)	Disintegration Time (Mins)	Weight Variation (%)	Assay (% Content)
F1	5.010±0.19	1.960	7.800±0.02	3.000±0.23	99.700
F2	5.150±0.38	10.960	7.300±0.75	2.900±0.81	104.500
F3	5.250±0.49	8.860	8.000±0.26	4.500±0.09	104.380
F4	5.280±0.15	0.870	7.800±0.33	1.300±0.04	100.770
F5	5.750±0.21	0.520	8.180±0.90	1.610±0. 0.03	104.000
F6	2.050±0.13	-	0.330±0.29	4.800±0.88	97.460
F7	3.510±0.41	17.140	0.320±0.07	2.800±0.90	100.700
F8	3.620±0.32	10.240	0.470±0.59	1.200±0.32	96.970
F9	3.760±0.07	3.750	0.420±0.78	0.750±0.77	101.370
F10	4.600±0.02	0.840	0.460±0.03	2.970±0.32	103.840

F11	2.500±0.20	7.210	0.370±0.05	1.400±0.12	104.380
F12	4.100±0.30	3.210	0.400±0.88	2.970±0.17	99.300
F13	4.300±0.03	0.810	0.490±0.49	2.870±0.09	102.880

4. CONCLUSION

From the outcomes of the research, it can be concluded that ethyl starch had less binding activity than the native and standard starch, but it has a good material property and higher purity than the native starch.

5. REFERENCES

1. Wallis T E .Text book of Pharmacognosy. 5th ed. NewDelhi: CBS Publications and Distributor; 1985; p. 7-19.
2. Wade A and Weller P J. Hand book of Excipients. 2nd edition. Washington: American Pharmaceutical Association; 1994; p. 483-488.
3. Newman A W, Muller R L, Vitez L M and Kiesnowsk C C . Starches and Starch derivatives. Encyclopedia of Pharmaceutical Technology. 2007; 10: 3476 – 82.
4. Bos CE, Bolhuis GK, Lerk CF, and Duineveld CAA(1992): Evaluation of modified Rice Starch: A New Excipient for Direct Compaction. *Drug Dev. Ind. Pharm*.; 18: 93-106.
5. Okafor I S, Ofoefule S I and Udeala O K. A comparative study of modified starches in direct compression of a water soluble drug chloroquine phosphate. Boll Chim Farm 2000; 139: 252-5.
6. Alves R M, Grossmann M V, Ferrero C, Zaritzky N E, Martino M N and Sierakoski M R. Chemical and functional characterization of products obtained from yam tubers. Starch 2002; 54: 476-481
7. Lawal O S, Lechner M D, Hartmann B and Kulicke W M.Carboxymethyl cocoyam starch: synthesis, characterization and influence of the reaction parameters. *Starch*/Sta"rke 2007; 59: 224 – 33
8. Association of Analytical Chemist.(1990). Official methods of analysis of AOAC international (16th Ed.). Gaithsburg, ML: Association of analytical chemist International.
9. Ohwoavworhua FO, Kunle OO, Ofoefule SI. Extraction and characterization of microcrystalline cellulose derived from Luffa cylindrical plant. Afri J Pharm Res Dev.; 2004; 1: 1 -6
10. Kornblum SS, Stoopak SB. A new tablet disintegrating agent: crosslinked polyvinyl pyrolidine. J Pharm Sci 1973; 62:43 -8.
11. Association of Analytical Chemist.(1990). Official methods of analysis of AOAC international (16th Ed.). Gaithsburg, ML: Association of analytical chemist International.
12. Guyot-Hermann A M. The disintegration and disintegrating agent. S.T.P. Pharmaceutical Science; 1992; 2: 445-62.
13. Mistry A H, Eckhoff S R. Characterization of alkali extracted starch obtained from corn flour. Cereal Chem 1992; 69: 296 – 303
14. Vasanthan T. Overview of laboratory isolation of starch from plant materials: Current protocols in food analytical chemistry. John wiley and sons incorporated, New York. 2001; pp. E2.1.1 - E2.1.6.
15. Gilbert S B and Christopher T R. Tablet dosage forms. Modern Pharmaceutics, 4th edition. Marcel Dekker Inc., New York. 2002; 1 - 450.

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