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Tableting and Evaluation of Paracetamol Tablets Formulated from Locally Sourced Dioscorea rotundata Starch

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Abstract
Starches are of great importance in the pharmaceutical industry for the manufacture of solid dosage forms especially tablets and capsules. Starches from different sources have been reported to be of great values and perform very well like maize starch BP. In this study, starch from white yam (*Dioscorea rotundata*) was extracted, characterized and its mucilage used as binder to formulate paracetamol tablets. The properties of the tablets were compared with tablets produced from maize starch BP. Seven batches of paracetamol tablets with different concentrations of the starch as binder were produced (F1=5% w/w, F2=7.5% w/w, F3= 10%w/w and F4=15% w/w. F5 on the other hand, contains 10% w/w of yam starch mucilage as binder and 5% w/w yam starch powder as disintegrant; F6 contains 10%w/w of maize starch BP as binder and 5%w/w maize starch BP as disintegrant; while F7 contains 10%w/w yam starch mucilage as binder and 10%w/w maize starch powder as disintegrant). The starch yield from the yam tuber after extraction was 74.59% and the pH was 6.8. The angle of repose of the formulated paracetamol granules for batches F1, F2, F4, F5 and F7 fell within 31^0- 35^0; indicating a good flow, while batches F3 and F6 was 36^0 - 40^0 indicating a fair flow. Batches F4 and F7 had the highest hardness values, while batch F1and F6 had highest percentage friability values - 1.20% and 1.02% respectively. Paracetamol tablets formulated from *Dioscorea rotundata* had comparable disintegration time and dissolution profile with tablets formulated with maize starch BP. The results obtained showed that, *Dioscorea rotundata* starch mucilage has good binding properties and could be modified into a high grade pharmaceutical starch and employ in the production of tablets.
Keywords: Starch, *Dioscorea rotundata*, binder.

1. Introduction

Root and tuber crops produce edible, fleshy underground storage organs which are rich in starch, sugar and varying amounts of other nutrients. They constitute the major source of daily carbohydrates intakes and serve as source of starch and sugar for industries. Starch is a polysaccharide produced by all green plants as energy store (Malami and Thompson, 2012). Starch, a major storage biopolymer synthesized by plants and constitutes a convenient means of storing large amounts of chemical energy and organic matter without altering the osmotic balance of the cells (Judith, 2012). Hence, the properties and utilization of this polysaccharide are of great interest. Starch is the most commonly used excipient in the pharmaceutical industry due to its interesting physical properties – e.g. disintegration and binding properties (Newman *et al*, 2007).

There is avalanche sources of starch for commercial use, however there is over dependent on few sources e.g. corn starch. Corn starch account for more than 80% of the world's sources of starch for industrial applications; most of which is produced in the United States of America (Bragamca and Fowler, 2004). China also has abundant raw materials for starch production, such as maize (103 million tons), cassava (4.4 million tons), wheat (106 million tons), potato (46 million tons) and sweet potato (113 million tons) per annum (Xiang, 1996).

Europe, a major producer of wheat and potato starches produces 17% of the world starch (Mweta, 2009). In Nigeria, starch is obtained from cereals, root and tuber crops.

Over dependent on corn starch in both the food and non – food industries has placed great pressure on the supply chain. To this effect, there is need for further research on starches from other sources such as white yams, *Dioscorea rotundata* for use as pharmaceutical excipients.

Yam is the common name for some plant species in the genus Dioscorea (family: Dioscoreaceaea) that form edible tubers. There are over 600 varieties of yam and these crops are grown in West Africa and Central Africa (Oluwatoyin 2012). The most economically important ones are: *Dioscorea rotundata*, Dioscorea opposite, *Dioscorea bulbifera, Dioscorea alata, Dioscorea esculanta, Dioscorea dumetorium and Dioscorea trifida* (Oluwatoyin, 2012). Yams are very good sources of starch; they are rich in starch, making up to 85% of the tuber. *Dioscorea rotundata* (often refers to as common yam or white yam) is of African origin, with a slightly or non-pigmented (creamy or white) flesh. It is cultivated in West Africa, especially in Nigeria (Ahmed *et al*, 2008). Its tuber has a rough skin usually light to dark brown in colour. This rough skin can be peeled with minimal degree of difficulty.

Dioscorea rotundata is made up of 67% moisture. By dry weight, the yam is composed of 80% starch, 7% protein, 7% minerals, 3% fiber and 1.7% lipids. 100 g of *D. rotundata* yields 385 Kcal energy (Ahmed *et al*,

2008).

In the present study, high grade pharmaceutical starch powder extracted from white yam (*Dioscorea rotundata* Prior) locally and evaluated for use as binder as an alternative to the well-established maize starch BP.

To achieve these objectives, starch was extracted from white yam, characterized and investigated as binder for paracetamol tablets manufacture

2. Materials and Methods

2.1.Materials

Yam starch, extracted locally from white yam, *D. rotundata* as test starch. The yam tubers were purchased from Abavo market, Delta State, Nigeria and authenticated by the plant curator, Botany Department, Delta State University, Abraka, Nigeria. Maize starch BP (BDH Chemicals, Poole England) as standard; Paracetamol (BDH Chemicals Poole England) is the test drug. 2% magnesium stereate and 2% talc (analytical grade) serve as lubricant and glidant respectively. All other reagents were used without further purification.

2.2. Methods:

Extraction of starch: The yam tubers were washed, weighed, peeled and cut to small bits. These were then ground with kitchen blending machine (Philips NL9206AD – 4 Drachten, China). The blended yam was diluted with water and sieved with a muslin cloth and allowed to stand for 2 h; after which, the supernatant was decanted carefully. Fresh water (about three times the volume of the filtrate) was added to it and re - suspended. After 2 h, the supernatant was again decanted and the starch sediments dried with hot - air oven at a temperature of 60 ± 0.5^0C for 12 h. The dried cakes were powdered, the weight noted and percentage yield computed with the formula:

$$\%\,Yield = \frac{W_1}{W_0} * \frac{100}{1} \quad ----------(1.1)$$

Where: W0 = weight of the yam tuber, W1 = weight of the dried starch.

Evaluation of the extracted starch

(a) The extracted starch was subjected to iodine test and mulish test to confirm the presence of polysaccharides (Kokate *et al*, 2010)

(b) Solubility test: The solubility of the extracted yam starch in cold water, methanol, ethanol, chloroform and hot water (at 60^0C, 80^0C and 100^0C) were determined and the results obtained recorded (Raymond *et al*, 2009).

(c) pH: 1 g of the extracted starch was dispersed in 100 ml distilled water and the pH determined with an electronic pH meter (Hanna Instrument; Model: HI2211) (Olayemi *et al*, 2008).

(d) Flow and packing properties: Flow and packing properties of the extracted starch were carried out by measuring the bulk and tapped densities and angle of repose.

(e) Swelling property: Starch suspension (5% w/v) was prepared at room temperature by dissolving 5 g of the starch powder in 100 ml of distilled water. The suspension was shaken for 5 min and sedimentation volume measured. The suspension was allowed to stand for 24 h and the swelling capacity was calculated as (Bharath *et al*, 2012):

$$Swellin\ capacity = \frac{V_0}{V_0} \quad ----------(1.2)$$

Where: V_0 = volume occupied by starch before dispersion, V_1 = final volume after 24 h

Preparation of paracetamol granules: Several batches of paracetamol granules (F1 to F7) were prepared with the wet granulation method according to the formula in Table 1. The extracted yam starch was formulated into mucilage and used as binder in batches F1, F2, F3, F4, F5 and F6; while in batch F7, the extracted yam starch powder was used as a disintegrant.

Appropriate amount of the various ingredients were weighed, mixed and kneaded with the mucilage and forced through a 1 mm sieve. The wet granules so formed were dried in a hot air oven at 60 ± 0.5^0C for 24 h. The dried granules were sieved with a 710 µm sieve and stored for further work.

Compression to tablets: The granules prepared above were mixed with 2% talc (glidant), 2% magnesium stearate (lubricant) and half of the disintegrant (maize starch) that were not used during granulation were added and compressed into tablets of 580 mg weight using a single punch tableting machine (Manesty, type F3) at a load of 30 arbitrary units.

Evaluation of tablets: (a) Disintegration test: The test was done using Manesty disintegration apparatus. Water maintained at 37 ± 0.5^0C was the disintegration medium. Six tablets were selected at random from each batch and the procedure being as described in the British Pharmacopeia (1998).

(b) Friability test: Ten tablets from each batch were placed in the drum of the friabulator (Erweka, Heusenstamm, Germany) rotating at 50 rpm for 5 min. The percentage weight lost due to the impact was

determined and taken as an index of friability. The test was done in triplicate and the mean values reported.

(c) Tensile strength (T): The tensile strength of the tablets was determined using multiple digital hardness test equipment (VDIGITAB – 1, Mumbai, India) by measuring the diameter (d), thickness (t), crushing load (p) and the weight of ten (10) tablets selected at random from each batch.

(d) Dissolution test: The in-vitro dissolution profile for each batch of the tablets was determined using a stirred beaker method described by previous researchers (Okor, 1989; Iwuagwu and Onyeonwu, 2002) was employed for this test. The dissolution medium consists of 900 ml freshly prepared 0.1 N hydrochloric acid solution maintained at 37 ± 0.5^0C. A tablet from each batch was placed in the dissolution medium and at interval of 10 min, 15 min, 30 min, 45 min, 60 min, 90 min and 120 min, samples (5 ml) were withdrawn and the fluid replaced with fresh dissolution medium. The samples were analyzed with a UV - Visible spectrophotometer (PG. Instrument) at a wave length of 245 nm.

TABLE 1: Formulae for preparation of the various paracetamol granules

Ingredients	**F_1**	**F_2**	**F_3**	**F_4**	**F_5**	**F_6**	**F_7**
Paracetamol (API) (mg)	500	500	500	500	500	500	500
D. rotundata starch (binder) (%w/w)	5	7.5	10	15	10	__	10
Maize starch (binder) (%w/w)	__	__	__	__	__	10	__
Maize starch (disintegrant) (% w/w)	5	5	5	5	__	5	10
D. rotundata starch (disintegrant) (%w/w)	__	__	__	__	5	__	__
Magnesium stearate (Lubricant) (% w/w)	2	2	2	2	2	2	2
Talc (Glidant) (% w/w)	2	2	2	2	2	2	2
TOTAL (mg)	580	580	580	580	580	580	580

TABLE 2: Flow properties of *Dioscorea rotundata* starch powder.

Parameters	**Values obtained**
Bulk density (g/ml)	0.625 ± 0.05
Tapped density (g/ml)	0.820 ± 0.02
Angle of repose (°)	43.22 ± 0.11
Carr's index (%)	23.78 ± 0.14
Hausner's ratio	1.32 ± 0.02

3. Results and Discussion

Results of starch evaluation: The percentage yield of the starch extracted from *D. rotundata* is 74.59%.

The starch was not soluble in cold water, hot water, methanol, ethanol and chloroform. However, the starch gels in hot water at 100^0C. Iodine test revealed blue black colouration. Mulish test produced a deep violet colour. Both results indicated presence of starch. The pH of the extracted starch was 6.8 which is in accordance with WHO values – 6.8 to 7.2 - (Malami and Thompson, 2012)

Flow and packing properties of the extracted starch: The results for angle of repose, bulk and tapped densities, Hausner's ratio and compressibility index values of the extracted starch are shown in Table 2. The angle of repose obtained indicates a passable flow that may hang up. This is a reflection of the nature of the starch powder: the fine particles and the interaction that exist. The compressibility index and Hausner's ratio indicated passable flow (USP, 2014).

Properties of Granules: Results of the characterization of the various granules are shown in Table 3. The tapped densities values were generally higher than the bulk densities for all the batches which are indication of good compaction characteristics (Joan, 2013).

The angle of repose obtained also indicated that batches F1, F2, F4, F5 and F7 had good flow since their angle of repose fell within the range: 31 – 35^0 while batches F3 and F6 had a fair flow (36 - 40^0). Angle of repose test results is reported to be very dependent upon the method used. Examples are abound in the literatures of formulations with angle of repose in the range of 40 – 50^0 that were manufactured satisfactorily (Uhumwangho and Okor, 2006; Avbunudiogba *et al*, 2013). When the angle of repose exceed 50^0, the granule is rarely acceptable for manufacturing processes (Analytical Laboratory, 2014).

Carr's index and Hausner's ratio obtained for all the batches indicated that the granules have poor flow. Carr's index for all the batches of paracetamol granules fell within 28 to 32%, while Hausner's ratio values ranged between 1.39 and 1.47. Granules have excellent flow when the compressibility index is less than 15%; while compressibility index above 25% indicates poor flow property (USP, 2014). Several factors could be responsible for poor granules flow. One of such factors is high interparticles interaction which in turn could be caused by several factors such as bulk density, size, shape, surface area, moisture content and cohesiveness of materials (Analytical laboratory, 2014). Alteration of these factors can improve granules flow. Hausner's ratio and Carr's index is an indication of the degree of densification that occurs during tableting. As these values

increase, the flow of the powder/granule decrease and gives more likelihood of producing tablets with more weight variability (Olayemi *et al*, 2008).

Results of tablets evaluation: Tablets friability percentage, hardness and disintegration time are shown in Table 4, while dissolution profiles are shown in Figure 1. Batches F4 and F7 had highest hardness values. This was expected as these two batches had highest concentration of the test starch (binder) – 15% w/w and 10% w/w respectively. Too hard a tablet may not disintegrate at the right time. The hardness of a tablet depends on the compression pressure and the type and concentration of the binding agent used (Musa *et al*, 2012). The same compression force was used for all the batches; therefore the differences in hardness probably resulted from the difference in binder concentration. Batches F5 and F6 had the same concentration of binder and disintegrant (10% and 5% respectively) but with starches from different botanical sources: *D. rotundata* and Zea mays respectively. Batch F5 tablets were slightly harder than batch F6 and as earlier stated, may be due to different source of starch.

Friability percentage: Batches F1 and F6 have friability values of 1.2% and 1.02% respectively. F2, F3, F4, F5 and F7 met the compendia specification for friability, with values less than 1%. F5 and F6 tablets had same concentration of binder and disintegrant but starches (binder) from different botanical sources. The results showed that F6 tablets were more friable than F5 tablets (1.02% and 0.68% respectively). Friability is a mechanical property of tablets which is a tool to check surface deformation of the tablets. It also showed how well a set of tablets can withstand abrasion.

Disintegration time: The tablets in batch F4 disintegrated slower than those of B6 indicating that the starch from *D. rotundata* provided more cohesive force than maize starch. Batch F7 tablets disintegrated faster compare with tablets from other batches. This is expected as it contains highest concentration of disintegrant.

TABLE 3: Pre-compression studies of formulation blend.

Batches	Bulk density (g/ml)± SD	Tap density (g/ml)± SD	Angle of repose(º)±SD	Carr's index (%)± SD	Hausner's ratio ± SD	Bulkiness ± SD	Flow rate (g/s) ± SD
F1	0.36 ± 0.01	0.53 ± 0.02	32.15 ± 0.07	31.33 ± 0.04	1.45 ± 0.05	2.77 ± 0.8	1.43 ± 0.01
F2	0.42 ± 0.00	0.61 ± 0.00	34.29 ± 0.04	31.93 ± 0.06	1.47 ± 0.05	2.40 ± 0.9	0.50 ± 0.00
F3	0.41 ± 0.00	0.60 ± 0.01	36.56 ± 0.08	31.50 ± 0.20	1.46 ± 0.13	2.40 ± 0.2	1.50 ± 0.00
F4	0.38 ± 0.00	0.57 ± 0.05	32.28 ± 0.08	32.05 ± 0.10	1.47 ± 0.06	2.60 ± 1.0	1.38 ± 0.00
F5	0.38 ± 0.01	0.54 ± 0.01	31.3 ± 0.06	28.21 ± 0.04	1.39 ± 0.07	2.60 ± 0.2	1.53 ± 0.08
F6	0.42 ± 0.00	0.59 ± 0.02	40.37 ± 0.05	29.16 ± 0.05	1.41 ± 0.02	2.40 ± 0.8	0.57 ± 0.00
F7	0.37 ± 0.01	0.51 ± 0.05	29.09 ± 0.10	28.47 ± 0.03	1.40 ± 0.03	2.70 ± 0.7	1.43 ± 0.01

Where SD = Standard deviation

Dissolution profiles: The dissolution profiles of the different batches formulated from *D. rotundata* starch and maize starch area shown in **Figure 1**. In virtually all the batches, up to 70% of the drug (paracetamol) was released within 45 min. This is in accordance with compendia specification for uncoated conventional tablets (BP, 2002).

Batch F5 released the drug more slowly than batch F6. From batches F1 to batch F4, the rate of release of the drug decreased as the binder concentration increased. Batch F7 had highest percentage drug release probably due to highest concentration of disintegrant.

Conclusions

Starch was successively extracted from yam (*Dioscorea rotundata*), evaluated for its physicochemical properties and used as binder/disintegrant for the production of paracetamol tablets – a highly patronized analgesic for mild/moderate pain. The results of this research reveal that starch from *D. rotundata* could compete favourably with maize starch BP as pharmaceutical excipients. However, further studies such as modification of the extracted starch should be carried out to obtain high grade starch for pharmaceutical use.

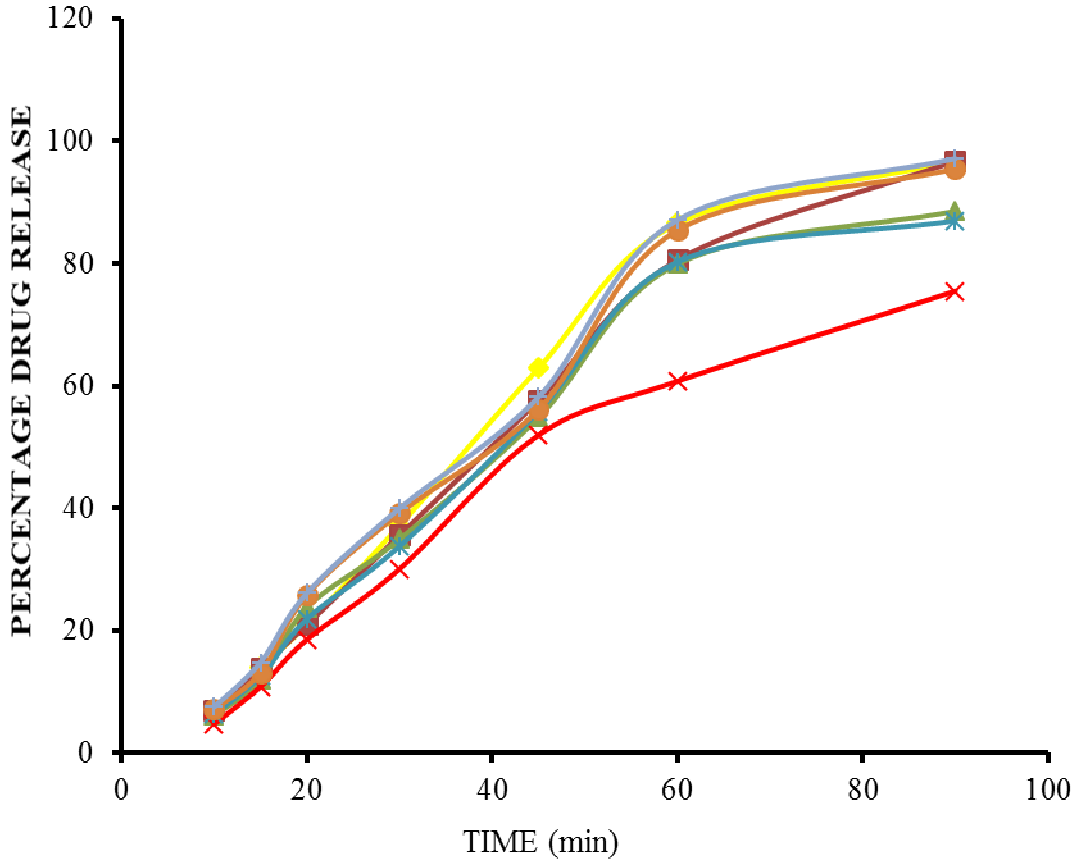

Fig 1: Drug release profile of the various batches of paracetamol tablets formulated from *D. rotundata* starch as binder: 5%w/w (—♦—), 7.5%w/w (—■—), 10%w/w (—▲—), 15%w/w (—X—). F6 has maize starch as binder (10%w/w, (—ж—) and F7 (10%w/w yam starch as binder and 10%w/w maize starch as disintegrant, ┼)

References

Ahmed, K. J., Olufemi, S. A., Simeon, A. A., Sikiru, A. B. and Adekule, B. O. (2008). Effect of food processing on glycemic response to white yam (Diocorea rotundata) meals. Diabetologia Croatica, 37(3): 67 – 72.

Analytical Laboratory (2014). Bulk and tapped density. Available on website; http://particle.dk/methods-analytical-laboratory/bulk-and-tapped-density/more-about-bulk-and-tapped-density/. (Accessed on 14th of April, 2014).

Avbunudiogba, J. A., Okor, R. S., Uhumwangho, M. U. and Arhewoh, M. I. (2012). Melt granulation of aspirin powder as an alternative to slugging: Implication for compressibility and dissolution rate. Nig. J. Pharm. Sci. 11(1): 23 – 30.

Bharath, S., Murali, P. K. R., Deveswaran, R., Basavaraj, B. V. and Madhava, v. (2012). Extraction of polysaccharide polymer from Dioscorea trifida and evaluation as tablet binder. Int. J. Pharm & Pharm Sci. 4(3): 347 -352.

Bragama, R. M. and Fowler, P. (2004). Industrial markets for starch. The biocomposite centre (online). Accessed on 28th May from http://www.bc.banor.ac.uk.

British Pharmacopoeia. (1998). HSMD, London.

British Pharmacopoeia. (2002). Monograph on disintegration times of coated tablets. Her Majesty's stationary office, London: Pg. A237.

Chitedze, J., Monjerezi, M., Kalenga Saka, J. D. and Steenkamp, J. (2012). Binding Effect of Cassava Starches on the Compression and Mechanical Properties of Ibuprofen Tablets. J. Applied Pharm. Sci. 2(4): 31 - 37

Iwuagwu, M.A. and Onyeowu, A. (2002). In vitro assessment of ampicillin capsules marketed in Nigeria. International Journal of Pharmacy Practice. 1(31):161-171

Kokate, C. K., Purohit, A. P. and Gokhate, S. B. (2010). Text book of Pharmacognosy, (38th ed.). Pune: Rachana enterprises, page 614 – 623.

Malami, S. and Thompson I. (2012). Physicochemical analysis of starch extracted from seeds of Faidherbia albida. J. Phy. Sci. & Inn. 4: 36 – 43

Musa, H., Gambo, A. and Bhatia, P.G. (2011). Studies on some physiochemical properties of native and

modified starches from Digitarna Iburua and Zea mays. Int J. Pharm and Pharma Sci. 3(1):28-31.

Mweta, D. E., Labuschangne, M. T., Koen, E., Benesi, I. R. M. and Saka, J. D. K. (2008). Some properties of starches from cocoyam (Colocasia esculenta) and cassava (Manihot esculenta Crantz) grown in Malawi. Africa. J. Food Sci. 2: 102 – 111.

Newman, A. W., Muller, R. L., Vitez, L. M. and Kiesnowsk, C. C. (2007). Starches and Starch derivatives. Encyclopedia of Pharmaceutical Technology. 10: 3476 – 3482.

Olayemi, O. J., Oyi, A. R., and Allagh, T. S. (2008). Comparative evaluation of maize, rice and wheat starch powder as pharmaceutical excipients. Nig. J. Pharm. Sci. 7(1): 131 – 138.

Okor, R. S. (1989). Modification of solute dissolution rate by coprecipitation with certain acrylate methacrylate co-polymers. Journal of Polymer Science. 37:1233 - 1238.

Oluwatoyin, A. O. (2012). Potentials of tropical excipients: A review. Starch Journal. 65: 89 – 106.

Raymond, C. R. and Paul, J. S. (2009). Hand book of Pharmaceutical excipients. 6th ed. Chicago, Pharmaceutical press. 478 – 479.

Uhumwangho, M. U. and Okor, R. S. (2006). Modification of drug release from acetaminophen granules by melt granulation technique – consideration of release kinetics. Pak. J. Pharm. Sci., 19(1): 22 – 27.

US Pharmacopoeia (2014), Dosage forms. Available on website; www.drugfuture.com/pharmacopoeia/usp32/pub/data/v32270/usp32nf27s0_c1151.html. (Accessed on 14th of April, 2014).

Xiang, Z. J. (1996). The present situation and prospects for further development of starch based industries in China. In Howeler, R. H., Oates, C. G. and O'Brien (eds). Cassava starch and starch derivatives. Proceedings of the International symposium held in Nanning, Guangxi, China. 12 – 19.Lawrence, S. *et al*. (2001). Persistence of Web References in Scientific Research. *Computer*. 34, 26-31. doi:10.1109/2.901164, http://dx.doi.org/10.1109/2.901164